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Submucosal fibroids and the relation to heavy menstrual bleeding and anemia

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Abstract

Objectives—To determine the contribution of submucosal fibroids to heavy menstrual bleeding (HMB) and anemia among women with HMB.

Study Design—Our retrospective study included premenopausal women, who presented to a tertiary care center for HMB between January, 2007 and October, 2011. All women in this cohort underwent flexible office hysteroscopy (n=1,665) and 259 (15.6%) had submucosal fibroids. We also reviewed clinical ultrasounds (n=914) from these women to determine if submucosal fibroids (n=148) or any fibroids (n=434) were present in the uterus. Clinical evaluation of bleeding included hemoglobin and pictorial blood loss assessment charts (PBLAC).

Results—In our cohort, hysteroscopically-diagnosed submucosal fibroids were associated with significantly lower hemoglobin (adjusted difference –0.35 g/dL (95% confidence interval (CI) –0.56 g/dL, –0.13g/dL) and higher risk of anemia (odds ratio (OR) 1.46, 95% CI 1.04, 2.03). Women with ultrasound-diagnosed submucosal fibroids had lower hemoglobin and anemia, but results were not significant once adjusted for confounders (hemoglobin: adjusted difference –0.21 g/dL, 95%CI –0.47g/dL, 0.06g/dL and anemia: OR 1.28, 95% CI 0.82, 1.97). Ultrasound-diagnosed fibroids anywhere in the uterus were not associated with hemoglobin (p=0.7) or anemia (p=0.8). Self-reported PBLAC scores did not differ between women with and without fibroids diagnosed by either hysteroscopy or ultrasound (p=0.4 & 0.9 respectively).

Conclusion—Submucosal fibroids were related to lower hemoglobin and higher risk of anemia, but not self-reported bleeding scores. Diagnostic modality was important: hysteroscopically-diagnosed submucosal fibroids had lower hemoglobin and more anemia than ultrasound-diagnosed submucosal fibroids. This may explain inconsistent results in the literature.

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Condensation:

Hysteroscopically-diagnosed submucosal fibroids are associated with lower hemoglobin and higher risk of anemia, but not higher bleeding scores.

Keywords

anemia; office hysteroscopy; pictorial blood loss assessment score; submucosal fibroid; ultrasound

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Introduction

Submucosal fibroids (SM) are presumed to cause heavy menstrual bleeding (HMB) leading to anemia; but not all research supports this. The definition of SM can vary from distorting the uterine cavity to being adjacent to it, and the classification depends on the diagnostic modality used. Hysteroscopy and sonohysterography are able to distinguish distortion of the uterine cavity better than ultrasound alone. Thus, studies that use hysteroscopy may define SM differently than those that use ultrasound.

Clinical studies indicate that the removal of SM that distort the uterine cavity will decrease HMB. Bleeding was controlled by myomectomy in 81% of women in one study¹ and 94% in a second study.² Studies of long-term outcomes of hysteroscopic myomectomy demonstrate a 14 – 86% improvement rate in HMB inversely related to fibroid size.^{3,4} However, other studies have not found an association between HMB and submucosal location. An ultrasound-based cross-sectional study concluded that size of the fibroid, but not submucosal classification, was related to gushing-type bleeding.⁵ A sonohysterography-based study found that both intramural fibroids and SM were fairly equally related to bleeding.⁶

The Mayo Clinic hysteroscopy database is a unique resource well-suited to determining the association of HMB and anemia due to SM. We hypothesized that hysteroscopically-diagnosed SM would contribute to lower hemoglobin, higher risk of anemia, and higher pictorial blood loss assessment chart (PBLAC) scores among women with HMB. We also hypothesized that ultrasound-diagnosed fibroids would have less impact on bleeding than hysteroscopically-diagnosed tumors and would depend on fibroid location. We have over 3,500 patients recorded that have undergone a hysteroscopic evaluation for abnormal uterine bleeding over the past five years. On these same women, we have systematically recorded the available clinical ultrasound data to compare with data from hysteroscopy.

Materials and Methods

We collected clinical data on women, who were treated by our physician group between January, 2007 and October, 2011. All women had undergone a flexible office hysteroscopy for evaluation of HMB (Figure 1). Institutional review board approved the protocol and only women who provided research authorization were included in the study. Demographic, clinical and laboratory variables were abstracted from the patient electronic medical records. During their clinical visit, participants were routinely asked about use of iron supplements and hormones and their risks of endometrial hyperplasia including obesity, infertility, diabetes, and hypertension. A standardized evaluation form was implemented early in 2009 to document these results. Office hysteroscopy was performed using flexible Olympus Hyf-XP (Tokyo, Japan) 3.1 mm scopes without local anesthesia (unless necessary or requested by patient) and using saline as the distending media. Saline was gravity fed with

intracavitary pressures of 50mmHg or less. Hysteroscopic diagnoses were categorized on visualization of cavity using 18 pre-determined diagnoses including submucosal fibroid. Inadequate hysteroscopies where visualization of the cavity did not occur were documented (n=10) and were excluded from analyses. The cohort was divided into women with any documented SM by hysteroscopy and those without any SM. The class of SM described by the surgeon was recorded using the European Society for Gynecologic Endoscopists' Classification System with class 0 being completely in the cavity, class 1 more than 50% in the cavity, and class 2 less than 50% in the cavity.²

Pictorial blood loss assessment chart (PBLAC) was used to document bleeding at the clinical visit. This is a validated measure of blood loss that asks women to quantify the number of tampons and pads used per day for each day in their cycle.⁷ The number of clots and menstrual accidents is also quantified and the weighted scores added together. A score of >100 corresponds to 80mL blood loss and represents HMB. Hemoglobin and iron store measures, including mean corpuscular volume and ferritin, were recorded when available from routine lab draws done within one year prior to or at the time of hysteroscopy. We performed a sensitivity analysis comparing PBLAC scores to anemia and hemoglobin to evaluate the relationship between the subjective and objective measures of bleeding.

Additionally, we collected data from patients in the hysteroscopy cohort who underwent ultrasound for clinical purposes within the past year. Standard protocol for ultrasound is to view and measure the fibroids in two views and document volume by cine clip. Type of fibroids (intramural, subserosal, and submucosal) was recorded from ultrasound reports. For missing data, images were reviewed and data recorded by one of two gynecologists (SKL, KP). Fibroids on ultrasound report that were listed as abutting, distorting or in the uterine cavity were classified as submucosal fibroids for this study. Thirty-six fibroids were listed as unknown and were reviewed by one of the authors (SKL). Three fibroids could not be classified and the other 33 were categorized based on image review.

The first comparison was made between women with ultrasound-diagnosed submucosal fibroids versus women with non-submucosal fibroids or no fibroids limited only to women with an ultrasound (to limit misclassification). Secondly, we compared women with any ultrasound-diagnosed fibroids (submucosal, intramural and subserosal) to those without fibroids limited only to women who had an ultrasound done.

Lastly, because all women with an ultrasound also had a hysteroscopy, we created a concordance variable that included women who had SM on both ultrasound and hysteroscopy. This concordance variable was then used to run a sensitivity analysis on the outcomes to determine if SM fibroids on ultrasound, confirmed by hysteroscopy, would lead to stronger bleeding outcomes.

Statistical analysis

Categorical and continuous data were analyzed using chi-square and student t-tests, respectively. Distributions of the continuous data were evaluated. Standard deviation is the method of dispersion reported for mean values of continuous data. PBLAC scores were skewed; thus, we used log transformation to compare groups and created categories to

display data. Categories were based on quantile. Univariate and multivariate analyses were performed for the outcomes of hemoglobin, anemia (defined as hemoglobin less than 12 g/dL), and PBLAC score >500. Step-wise backward regression models were used to determine significant co-variables for each set of analyses. For the continuous outcome of hemoglobin, a generalized linear model (Gaussian link) was used such that the outcome is reduction in hemoglobin (g/dL). For the binary outcomes of anemia and PBLAC score, a logistic regression model was performed. Significance level was set at p value <0.05. For the 259 women with hysteroscopically-diagnosed fibroids, we had an 88% power to detect a difference of 0.5g/dL hemoglobin using a two-sided t-test with a type I error rate of 5%. The power was >90% for the same testing for women with ultrasound-diagnosed SM.

Results

Over 3,500 women had an office hysteroscopy between January 1, 2007 and October 21, 2011. More than 98% of the hysteroscopies were performed by one of five physicians following a standard protocol. The 1,746 women who had a hysteroscopy performed for the indication of HMB were included in this cohort. Women who did not provide research authorization (n=71) were excluded and ten hysteroscopies were inadequate leaving 1,665 for analysis (Figure 1). Mean age of women undergoing hysteroscopy was 43.18 +/- 6.85, mean BMI 29.14 +/- 7.87, and most were multigravid and multiparous (Table 1). Participants were able to have indications for hysteroscopy in addition to HMB; irregular menstrual bleeding (IMB) was the most common (n=390). Nearly 70% reported pain during menses; however, data on painful menses were missing for 30% of the women.

Submucosal fibroids diagnosed by hysteroscopy

In this cohort, 259 women (15.6%) were diagnosed with SM by hysteroscopy. Sixty-three were class 0, 110 were class 1, 52 were class 2, and 25 were not documented by the physician. Women with SM were significantly older and were more likely to be nulliparous (Table 1). They were more likely to be using hormones or iron therapy. IMB was significantly more common for women without SM, but painful menses did not differ between groups.

Women with SM had lower hemoglobin (difference in mean 0.5g/dL, $p<0.001$, Table 1) and were significantly more likely to have anemia (38.29% vs. 26.91%, $p=0.001$). Multiple measures of iron deficiency including ferritin and MCV were consistent with these findings. In multivariate analyses (Table 2), SM were associated with a lower hemoglobin (adjusted difference -0.35, 95% CI -0.56, -0.13, $p=0.002$) and an increased odds ratio for anemia (adjusted OR 1.46, 95% CI 1.04, 1.97, $p=0.03$). Both hemoglobin and anemia showed trends by the class of SM (Table 3). Hemoglobin was negatively associated with class 0 fibroids (adjusted difference -0.45 g/dL, 95% CI -0.86, -0.05, $p=0.03$) and class 1 fibroids (adjusted difference -0.39 g/dL, 95% CI -.71, -0.08, $p=0.01$) when compared to women without SM. Similarly, the risk of anemia was increased with class 0 fibroids (adjusted OR 1.83, 95% CI 1.00, 3.36, $p=0.05$) and non-significantly with class 1 fibroids (adjusted OR 1.52, 95% CI 0.93, 2.48).

PBLAC scores did not differ between women with and without hysteroscopically-diagnosed SM (612 vs. 566 respectively, $p=0.3$). The proportion of women reporting a PBLAC score above 500 was similar between groups (38.57% vs. 41.27%, $p=0.5$, Table 1). SM were not associated with a PBLAC score over 500 in adjusted multivariate analyses (adjusted OR 1.15, 95% CI 0.83, 1.59, $p=0.4$, Table 2). PBLAC scores did not differ from women without fibroids for class 0 or class 1 SM. PBLAC score greater than 500 was associated with class 2 SM (adjusted OR 2.01, 95% CI 1.03, 3.93, $p=0.04$).

Submucosal fibroids by ultrasound

For clinical reasons usually associated with HMB, 914 women had an ultrasound within one year of the hysteroscopy and were recorded in our database. Nearly half were diagnosed with fibroids ($n=434$, 47.59%) and 148 (16.23%) had at least one SM (Table 4). Hormone use and painful menses were not different between groups. IMB was more common in women without ultrasound-diagnosed SM (25.52% vs. 16.22%, $p=0.02$). Iron use was more common among women with SM (27.03 vs. 19.58, $p=0.04$).

Hemoglobin was significantly lower among women with ultrasound-diagnosed SM (12.32 vs. 12.63, $p=0.02$, Table 4). Hemoglobin was negatively associated with ultrasound-diagnosed SM in the univariate analysis and in the analysis excluding adjustment for iron (-0.28 g/dL, 95% CI -0.56 , -0.01), but was not significant after adjusting for all significant co-variables (adjusted difference -0.21 g/dL, 95% CI -0.47 , 0.06 , Table 2). Anemia was more common among women with ultrasound-diagnosed SM (33.59% vs. 25.22%, $p=0.05$, Table 4). Anemia was associated with ultrasound-diagnosed SM in the univariate analyses, but not in the multivariate analyses (OR 1.28, 95% CI 0.82, 1.97, Table 2).

PBLAC scores were not different between women with and without ultrasound-diagnosed SM, and similar proportions of women reported PBLAC scores above 500 (38.93% vs. 41.12%, $p=0.7$, Table 4). Ultrasound-diagnosed SM and PBLAC scores were not associated in either unadjusted or adjusted models (Table 2).

Any fibroids diagnosed by ultrasound

For women with fibroids of any type diagnosed by ultrasound ($n=434$) vs. women without fibroids on US ($n=478$), hormone use and iron use were not different. IMB was more common in women without fibroids (29.33% vs. 18.16%); however, painful menstrual bleeding was not different between groups.

Hemoglobin did not differ between groups (12.60 g/dL vs 12.55 g/dL, $p=0.6$, Table 4). The proportions of women with anemia were similar between groups (25.30% vs. 27.98%, $p=0.4$). Fibroids by ultrasound were not associated with lower levels of hemoglobin (adjusted difference 0.04 g/dL, 95% CI -0.16 , 0.25) or anemia (OR 0.96, 95% CI 0.68, 1.37, Table 2).

PBLAC scores were similar between women with and without fibroids by ultrasound. The proportions of women that reported PBLAC scores greater than 500 were similar between groups (37.60% vs. 41.19%, Table 4). Fibroids were not associated with a PBLAC score greater than 500 (Table 2).

Sensitivity analyses

Using the concordance variable to evaluate ultrasound diagnosed SM, confirmed by hysteroscopy (n=86), results did not change. Hemoglobin and anemia were significant in univariate analyses, but not significant once adjusted for confounders. PBLAC scores were not related. Additionally, the SM by ultrasound were divided into levels of submucosal component (distorting endometrium, slightly displacing, and adjacent or abutting endometrium) and no difference in PBLAC or anemia were seen by these groups.

PBLAC scores were related to hemoglobin in linear regression analysis ($p=0.001$), indicating that PBLAC scores are useful in diagnosing heavy bleeding. Similarly, anemia was related to PBLAC scores (OR 1.47, 95% CI, 1.13, 1.91, $p=0.004$). Mean PBLAC score in women without anemia was 567.8 (SD 556.6) and for women with anemia 779.3 (SD 778.8).

Comment

The definition of SM and the diagnostic modality used may influence the outcome of fibroid research. If classifications of fibroids vary between studies, the results on effects of SM may be inconsistent. Hysteroscopically-diagnosed fibroids all distort the cavity, making the classification of SM fairly uniform and can be further classified into class 0, 1, or 2 fibroids for even finer comparisons. Ultrasound-based definitions of SM can vary from distorting the endometrium to being adjacent to the endometrium. Alternatively, some studies classify fibroids that are adjacent to the endometrium as intramural fibroids or classify large fibroids as intramural even if they distort the endometrium.

These inconsistencies occur frequently in the literature. In our study, lower hemoglobin and anemia were associated with hysteroscopically-diagnosed SM and stronger trends were seen for class 0 and 1 fibroids. Associations were not as strong for ultrasound-diagnosed SM, even when we used stricter definitions of SM on ultrasound in this cohort. Similarly, three studies that used ultrasound or MRI as a primary means of determining submucosal location did not find an association with bleeding.^{8–10} A fourth study using MRI found HMB in all SM, but also in the intramural fibroids, most of which distorted the uterine cavity.¹¹ The final study using hysteroscopy did find a relationship between the amount of protrusion of the fibroid into the cavity and anemia.¹² Our findings are consistent with this latter study and with radiologic studies that demonstrate the superiority of hysteroscopy over ultrasound in ruling out intrauterine abnormalities.¹³

Clinically, any fibroids in the uterus are often considered responsible for HMB, even if they do not affect the uterine cavity. However, we found no difference in hemoglobin, risk of anemia, and PBLAC scores in women with ultrasound-diagnosed fibroids of all types when compared to women without fibroids in this HMB cohort. HMB is multi-factorial and fibroids may not always contribute to greater bleeding, especially if distant from the uterine cavity. Because we grouped subserosal and intramural fibroids, it is possible that subserosal fibroids decreased the impact of intramural fibroids on the results.

Our findings also support the lack of correlation of self-reported bleeding scores to SM among women with HMB. In the two studies that used only self-reported bleeding scores^{8, 9} and not a more objective measure such as the alkaline hematin method or anemia, there was no relation between bleeding and SM. In two of three studies that used either anemia or the alkaline hematin method, associations were found.^{11, 12} In our cohort, PBLAC scores were not related to fibroids using any diagnostic modality for fibroids. PBLAC scores may not be able to differentiate HMB due to fibroids, among a cohort of women reporting heavy menstrual bleeding. Also, PBLAC scores are limited by a lack of standardization of sanitary products in terms of size and absorbency. For our study, PBLAC score was assessed at the clinic visit and thus, affected by recall bias.

While PBLAC scores were initially validated as accurate measures of blood loss,^{7, 14} a later study was unable to validate the PBLAC finding a specificity of only 7.5%.¹⁵ We were able to find a relationship between PBLAC and objective methods of bleeding: hemoglobin and anemia. However, the effect size of regression for hemoglobin on PBLAC, was small (Beta -0.0003) and would be difficult to see in studies with smaller sample sizes. Hemoglobin and anemia may be more objective for these studies.

The strengths of our study include the size of the cohort and the standardization of recording hysteroscopic findings among a small group of physicians. Our systematic recording of the hysteroscopy, ultrasound, laboratory and clinical data allows for analysis of multiple diagnostic modalities. Sample size was adequate to find expected differences even in our smallest comparisons (ultrasound-diagnosed SM). However, our study is not without limitations. The cohort is limited to women who had both HMB and underwent a hysteroscopy, which may bias the sample. The retrospective nature of the study also may lead to bias and limits the data available to those collected for clinical purposes. For instance, the role of iron in both the diagnosis of fibroids and anemia is complicated. Due to the retrospective nature of the study, the timing of the onset of fibroids versus the anemia could not be assessed. Thus, we ran the adjusted models both with and without iron. Iron use attenuated the results, which were still in the same direction of effect but non-significant. Additionally, the use of NSAIDs was not standardized, and the amount used per menstrual cycle, which may decrease menstrual bleeding in some women, was not quantified in clinical notes. We attempted to overcome biases by including all women with HMB and including all clinical data available.

We found evidence that SM contribute to heavier bleeding leading to anemia among women with HMB, and that the diagnostic modality used to define SM is key to determining clinical symptoms. These findings are important to the clinical association of other symptoms, such as infertility, with SM. Self-reported bleeding scores are not as effective as hemoglobin and anemia in determining the severity of HMB related to fibroids.

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References

1. Loffer FD. Improving results of hysteroscopic submucosal myomectomy for menorrhagia by concomitant endometrial ablation. *Journal of Minimally Invasive Gynecology*. 2005; 12:254–60. [PubMed: 15922984]
2. Wamsteker K, Emanuel MH, De Kruif JH. Transcervical hysteroscopic resection of submucous fibroids for abnormal uterine bleeding: results regarding the degree of intramural extension. *Obstet Gynecol*. 1993; 82:736–40. [PubMed: 8414318]
3. Makris N, Vomvolaki E, Mantzaris G, Kalmantis K, Hatzipappas J, Antsaklis A. Role of a bipolar resectoscope in subfertile women with submucous myomas and menstrual disorders. *J Obstet Gynaecol Res*. 2007; 33:849–54. [PubMed: 18001453]
4. Marziani R, Mossa B, Ebano V, Perniola G, Melluso J, Napolitano C. Transcervical hysteroscopic myomectomy: long-term effects on abnormal uterine bleeding. *Clin Exp Obstet Gynecol*. 2005; 32:23–6. [PubMed: 15864931]
5. Wegienka G, Baird DD, Hertz-Picciotto I, et al. Self-reported heavy bleeding associated with uterine leiomyomata. *Obstet Gynecol*. 2003; 101:431–7. [PubMed: 12636944]
6. Clevenger-Hoeft M, Syrop CH, Stovall DW, Van Voorhis BJ. Sonohysterography in premenopausal women with and without abnormal bleeding. *Obstetrics and Gynecology*. 1999; 94:516–20. [PubMed: 10511351]
7. Janssen CA. A simple visual assessment technique to discriminate between menorrhagia and normal menstrual blood loss. *European journal of obstetrics, gynecology, and reproductive biology*. 1996; 70:21–2.
8. Wegienka G, Baird DD, Hertz-Picciotto I, et al. Self-reported heavy bleeding associated with uterine leiomyomata. *Obstetrics and Gynecology*. 2003; 101:431–37. [PubMed: 12636944]
9. Marino JL, Eskenazi B, Warner M, et al. Uterine leiomyoma and menstrual cycle characteristics in a population-based cohort study. *Human Reproduction*. 2004; 19:2350–55. [PubMed: 15242998]
10. Bachmann GA, Bahouth LA, Amalraj P, Mhamunkar V, Hoes K, Ananth CV. Correlations of Anemia and Pain to Fibroid Location and Uterine Weight. *J Reprod Med*. 2011; 56:463–66. [PubMed: 22195327]
11. Sulaiman S, Khaund A, McMillan N, Moss J, Lumsden MA. Uterine fibroids--do size and location determine menstrual blood loss? *Eur J Obstet Gynecol Reprod Biol*. 2004; 115:85–9. [PubMed: 15223171]
12. Yang J-H, Chen M-J, Chen C-D, Chen C-L, Ho H-N, Yang Y-S. Impact of submucous myoma on the severity of anemia. *Fertil Steril*. 2011; 95:1769–72. e1. [PubMed: 21324448]
13. Dueholm M, Lundorf E, Hansen ES, Ledertoug S, Olesen F. Evaluation of the uterine cavity with magnetic resonance imaging, transvaginal sonography, hysterosonographic examination, and diagnostic hysteroscopy. *Fertil Steril*. 2001; 76:350–357. [PubMed: 11476785]
14. Higham JM, O'Brien PM, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. *British Journal of Obstetrics and Gynaecology*. 1990; 97:734–9. [PubMed: 2400752]
15. Reid PC, Coker A, Coltart R. Assessment of menstrual blood loss using a pictorial chart: a validation study. *BJOG : an international journal of obstetrics and gynaecology*. 2000; 107:320–2. [PubMed: 10740326]

Clinical Implications

- Submucosal fibroids contribute to lower hemoglobin and more anemia among women with heavy menstrual bleeding
- Hysteroscopically-diagnosed submucosal fibroids are associated with greater anemia and lower hemoglobin than fibroids diagnosed by ultrasound
- Proportion of fibroid that interrupts the cavity is related to greater hemoglobin loss and more anemia
- Blood loss assessment was not related to the presence of fibroids among women with heavy menstrual bleeding

Figure 1.**Office hysteroscopy flowchart**

Description: Flowchart of the women with office hysteroscopy for heavy menstrual bleeding included in our analyses of submucosal fibroids. Clinical data on ultrasounds are included with data on any fibroids and submucosal fibroids.

Table 1

Demographics and bleeding parameters for women with hysteroscopically-diagnosed submucosal fibroids (SM) versus no submucosal fibroids.

Fibroids by hysteroscopy				
<i>Demographic Factors</i>				
Factor	No SM	SM	Total	P value
N (%)	1,406 (84.4%)	259 (15.6%)	1,665	
Age (Mean, SD)	42.83 (6.98)	45.07 (5.76)	43.18 (6.85)	P<0.001
Gravida				P=0.08
0	166 (11.86)	41 (15.89)	207 (12.48)	
1	127 (9.07)	29 (11.24)	156 (9.41)	
2+	1,107 (79.07)	188 (72.87)	1,295 (78.11)	
Missing	6	1	7	
Para				P<0.001
0	205 (14.72)	58 (22.57)	263 (15.94)	
1	130 (9.33)	34 (13.23)	164 (9.94)	
2+	1,058 (75.95)	165 (64.20)	1,223 (74.12)	
Missing	13	2	15	
BMI (mean, SD)	29.28 (7.92)	28.39 (7.56)	29.14 (7.87)	P=0.1
Hormone use				p<0.001
No	1,164 (84.65)	185 (72.83)	1,349 (82.81)	
Yes	211 (15.35)	69 (27.17)	280 (17.19)	
Missing	31	5	36	
Iron Use				P<0.001
No	1,133 (80.81)	182 (70.27)	1,315 (79.17)	
Yes	269 (19.19)	77 (29.73)	346 (20.83)	
Missing	4	0	4	
Metrorrhagia				

	No	1,054 (74.96)	221 (85.33)	1,275 (76.58)	P<0.001
	Yes	352 (25.04)	38 (14.67)	390 (23.42)	
Dysmenorrhea	No	310 (31.16)	48 (30.00)	358 (31.00)	P=0.8
	Yes	685 (68.84)	112 (70.00)	797 (69.00)	
	Missing	411	99	510	
<i>Bleeding parameters</i>					
Hemoglobin (mean, SD)		12.62 (1.48)	12.12 (1.70)	12.54 (1.52)	P<0.001
Anemia	No	888 (73.09)	137 (61.71)	1,025 (71.33)	P=0.001
	Yes	327 (26.91)	85 (38.29)	412 (28.67)	
	Missing	191	37	228	
PBLA C ₅₀₀	No	680 (61.43)	111 (58.73)	791 (61.03)	P=0.5
	Yes	427 (38.57)	78 (41.27)	505 (38.97)	
	Missing	299	70	369	

Table 2

Univariate and multivariate models for bleeding parameters

Bleeding parameter	Unadjusted difference	Adjusted difference ^a	Adjusted difference ^b	P-value(adj) ^b
HEMOGLOBIN				
SM by hysteroscopy ^c	-0.49 (-0.71, -0.28)	-0.45 (-0.68, -0.23)	-0.35 (-0.56, -0.13)	0.002
SM by US ^c	-0.31 (-0.58, -0.05)	-0.28 (-0.56, -0.01)	-0.21 (-0.47, 0.06)	0.1
Any fibroids by US ^c	-0.05 (-0.25, 0.14)	0.01 (-0.20, 0.22)	0.04 (-0.16, 0.25)	0.7
	Unadjusted OR	Adjusted OR ^a	Adjusted OR ^b	P-value(adj) ^b
ANEMIA				
SM by hysteroscopy ^d	1.68 (1.25, 2.27)	1.62 (1.18, 2.24)	1.46 (1.04, 2.03)	0.03
SM by US ^c	1.50 (1.00, 2.24)	1.38 (0.90, 2.10)	1.28 (0.82, 1.97)	0.3
Any fibroids by US ^c	1.15 (0.84, 1.57)	1.01 (0.72, 1.42)	0.96 (0.68, 1.37)	0.8
PBLAC >500				
SM by hysteroscopy ^e	1.12 (0.82, 1.53)	1.16 (0.84, 1.61)	1.15 (0.83, 1.59)	0.4
SM by US ^f	1.10 (0.72, 1.67)	1.05 (0.68, 1.62)	1.03 (0.67, 1.59)	0.9
Any fibroids by US ^e	1.16 (0.85, 1.58)	1.12 (0.80, 1.56)	1.10 (0.79, 1.53)	0.6

^a adjusted models not including iron use^b adjusted models including iron use^c adjusted for age, parity, hormone use, IMB^d adjusted for age, parity, hormone use, IMB, and BMI^e adjusted for parity, IMB and BMI^f adjusted for parity, IMB

Table 3

Bleeding parameters by class of submucosal fibroid

	Class 0	Class 1	Class 2	Non-SM fibroid
Hemoglobin *	11.99 (1.75)	12.11 (1.87)	12.41 (1.32)	12.62 (1.47)
Anemia *				
No	30 (56.60)	59 (61.46)	32 (72.73)	900 (73.05)
Yes	23 (43.40)	37 (38.54)	12 (27.27)	332 (26.95)
Missing	10	14	8	192
PBLAC ≤ 500				
No	28 (63.64)	52 (60.47)	16 (43.24)	690 (61.72)
Yes	16 (36.36)	34 (39.53)	21 (56.76)	428 (38.28)
Missing				

*
p<0.05 for comparison among groups

Table 4

Ultrasound-diagnosed fibroids and bleeding parameters

<i>Submucosal Fibroids</i>				
Bleeding parameter	No SM (N=764)	SM (N=148)	Total (N=912)	P value
Hemoglobin (mean, SD)	12.63 (1.37)	12.32 (1.71)	12.58 (1.43)	0.02
Anemia				0.05
No	507 (74.78)	87 (66.41)	594 (73.42)	
Yes	171 (25.22)	44 (33.59)	215 (26.58)	
Missing	86	17	103	
PBLAC $\geq$ 500				0.7
No	353 (61.07)	63 (58.88)	416 (60.73)	
Yes	225 (38.93)	44 (41.12)	269 (39.27)	
Missing	186	41	227	
<i>Uterine Fibroids of any type (submucosal, intramural and subserosal)</i>				
Bleeding parameter	No Uterine Fibroids (N=478)	Uterine Fibroids (N=434)	Total (N=912)	P-value
Hemoglobin (mean, SD)	12.60 (1.43)	12.55 (1.43)	12.58 (1.43)	0.6
Anemia				0.4
No	316 (74.70)	278 (72.02)	594 (73.42)	
Yes	107 (25.30)	108 (27.98)	215 (26.58)	
Missing	55	48	103	
PBLAC $\geq$ 500				0.3
No	229 (62.40)	187 (58.81)	416 (60.73)	
Yes	138 (37.60)	131 (41.19)	269 (39.27)	
Missing	111	116	227	