American Journal of Obstetrics and Gynecology

Volume 198, Issue 2, February 2008, Pages 163.e1-163.e8

Development of a screening tool for identifying women with menorrhagia for hemostatic evaluation

Claire S. Philipp MD[a], Ambarina Faiz MD, MPH[a], Nicole F. Dowling PhD[d], Michele Beckman MPH[d], Sally Owens RN[d], Charletta Ayers MD, MPH[b] and Gloria Bachmann MD[b, c]

[a] Division of Hematology, Department of Medicine, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ
[b] Department of Obstetrics and Gynecology, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ
[c] Women's Health Institute, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ
[d] National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA.
Received 26 March 2007; revised 30 June 2007; accepted 28 August 2007. Available online 26 January 2008.

Objective

A study was conducted to develop a short, easy to administer screening tool useful for stratifying women with unexplained menorrhagia for hemostatic testing for underlying bleeding disorders.

Study Design

One hundred forty-six women with a physician diagnosis of menorrhagia underwent comprehensive hemostatic testing for the diagnosis of bleeding disorders, including von Willebrand disease, platelet dysfunction, and coagulation factor deficiencies. A 12 page questionnaire of bleeding symptoms was administered. Bleeding symptoms with high predictive values for laboratory hemostatic abnormalities were combined and used as single variables to calculate sensitivity, specificity, and positive and negative predictive values in order to develop a short screening tool to identify females for testing and evaluation.

Results

A combination of 8 questions in 4 categories resulted in a sensitivity of 82% (95%CI 75-90) for bleeding disorders. Adding a pictorial blood assessment chart score > 100 increased the sensitivity of the screening tool to 95% (95%CI 91-99).

Conclusion

These results demonstrate the feasibility of a simple questionnaire based screening tool to identify females for testing and evaluation for bleeding disorders.

Underlying bleeding disorders, including von Willebrand disease,[1], [2], [3], [4], [5] and [6] platelet dysfunction,[4], [7], [8] and [9] and other coagulation factor deficiencies[1], [2], [4] and [9] are prevalent in women presenting with menorrhagia. Recent studies demonstrate that while the prevalence of von Willebrand disease in the general population is reported to be approximately 1%,[10] the prevalence in women presenting with menorrhagia ranges from 5-24%.[6] Platelet dysfunction has been reported in approximately 50% of women with unexplained menorrhagia[4] and [7] and single factor deficiencies, such as factor XI, V, and VII deficiencies are also observed in approximately 1-4% of females with menorrhagia.[1], [2] and [4]

Comprehensive hemostatic evaluation for bleeding disorders, including von Willebrand disease, platelet dysfunction, and coagulation factor deficiency, is expensive, labor intensive, requires technical expertise for the performance and interpretation of results, and is usually performed in specialized coagulation laboratories. Platelet function testing requires fresh specimens and testing must be performed within a limited time of the blood draw, requiring close proximity of the specialized laboratory. Furthermore, transportation and processing artifacts can affect testing of von Willebrand and coagulation factor deficiencies.[11] Since bleeding disorders cannot be diagnosed by any one test, or combination of routine, easily available laboratory testing, testing, and evaluation for underlying bleeding disorders generally requires referral to a hematologist or specialized hemophilia treatment center. This is consistent with a recent ACOG Committee Opinion on menstruation in adolescents recommending consideration of hemostatic disorders in patients presenting with menorrhagia and hematologic or hemophilia treatment center referral for appropriate testing.[12]

Approximately 5% of women annually seek medical care for menorrhagia,[1], [13] and [14] and approximately 30% of women complain of heavy menses.[15] In approximately 50% of women, no organic pathology is determined.[15] and [16] Given the large number of women presenting with menorrhagia, however, referring all females with otherwise unexplained heavy menstrual flow for hemostatic evaluation would be difficult from the public health perspective and not cost effective, especially since a significant number of these women are found to have no abnormality on comprehensive testing. The availability of simple screening tools to assist the practicing gynecologist in determining which women to refer for comprehensive hemostatic evaluation would be useful. In this study, we evaluated the effectiveness of screening questions in order to develop a short questionnaire-based screening tool that could be implemented in outpatient settings to identify which females with menorrhagia might benefit from further hemostatic testing. The effectiveness of incorporating into a screening tool the pictorial blood assessment chart (PBAC), a measurement of menstrual blood loss, and the platelet function analyzer (PFA-100, Dade-Behring, Deerfield, IL), a rapid in vitro test of von Willebrand factor and platelet function, was also evaluated.

Materials and Methods

Females between the ages of 13 and 55 receiving a physician diagnosis of menorrhagia by the faculty gynecology practice of UMDNJ-Robert Wood Johnson Medical School or collaborating community gynecology and pediatric practices were eligible to participate. Women with the diagnosis of menorrhagia were identified through their medical record or gynecology provider. Women were excluded from participation if they had previously diagnosed bleeding or endocrine

disorders or had undergone a hemostatic evaluation, submucous uterine myoma, uterine polyps, malignancy, use of an intrauterine device, or treatment with anticoagulants within the past 2 months. Use of oral contraceptives within 1 cycle of participation and use of nonsteroidal antiinflammatory agents, aspirin, or other platelet-impairing medications or agents within 14 days of participation was not permitted in order to eliminate potential effects on hemostatic test results. A pelvic examination was required for all women 19 years or older. Women with intramural and subserosal fibroids were not excluded.

Informed consent, approved by the Institutional Review Boards of UMDNJ-Robert Wood Johnson Medical School and the Centers for Disease Control and Prevention, was obtained from study participants or their parent/legal guardian for subjects under 18 years old. Assent was also obtained from study participants less than 18 years old. A blood sample was obtained in participants between days 3-9 of their menstrual cycle.

Hemostasis testing

Testing for von Willebrand disease, platelet function defects, and coagulation factor deficiencies was performed as previously described.[7] Briefly, von Willebrand factor antigen (VWF:Ag) was measured by ELISA (Asserachrom VWF, Diagnostica Stago, Parsippany, NJ). Von Willebrand ristocetin cofactor (VWF:RCo) was measured by aggregation of lyophilized normal platelets. Factor VIII was measured by 1 stage assay on an automated analyzer (STAR, Diagnostica Stago). Platelet aggregation and ATP release were performed using platelet rich plasma on an optical platelet lumi-aggregometer (Chrono-Log Corp, Haverton, PA). Coagulation factors II, VII, V, IX, X, XI, and XII were performed using factor deficient plasmas. All samples were tested in duplicate.

PFA-100 closure times were determined using the collagen/epinephrine (CEPI) and collagen/ADP (CADP) cartridges (Dade-Behring, Deerfield, IL). PFA-100 testing with each cartridge was performed in duplicate, as previously described.[17]

Pictorial chart assessment of menorrhagia

At the time of their study visit, women were provided a pictorial chart to complete with their next menses and an explanation of how it should be completed. Using the pictorial charts, lightly, moderately, and heavily soiled pads and tampons were recorded for the entire menstrual flow. Clots were also recorded in comparison with coins as previously described.[7], [18] and [19] Women were not receiving treatment for menorrhagia when the PBAC was recorded.

Questionnaire

A 12-page questionnaire was administered to all study participants at the time of the study visit. The questionnaire was based on the bleeding symptoms that were found significant in women with diagnosed von Willebrand disease compared to friend controls.[20] Questions assessing the severity of menstrual bleeding, other bleeding symptoms, excessive bleeding after tooth extraction, surgery, or delivery, and a history of anemia or its treatment were included. In addition, questions assessing a family history of bleeding symptoms and family diagnosis of bleeding disorder were also queried. Each question in the questionnaire had a precoded response, which was either “yes” or “no” for the questions pertaining to the presence or absence of certain symptoms or a number for the questions pertaining to the frequency of bleeding episodes. The questionnaire had several “contingency questions” that were relevant to certain women but were irrelevant to others. For these questions, if the response was “yes,” women were asked subsequent questions; responses to these subsequent questions were contingent on the response

to the first question. If the response was “no” to that question then subsequent questions were skipped.

Coding of questionnaire

All questionnaire responses, whether “yes/no” or numerical, were coded to represent excessive bleeding that would be considered clinically significant. For “yes/no” responses, “yes” responses were coded as abnormal and “no” responses were coded as normal. Frequency or duration of symptoms was coded to be compatible with clinically defined excessive bleeding. For example, duration of menses was coded as “0” or “normal” if bleeding lasted less than 7 days but as “1” or “abnormal” if the duration of the menses was equal to or more than 7 days.

Hemostatic abnormalities

Hemostatic disorders were defined as platelet function defects, decreased von Willebrand factor (VWD), and/or coagulation factor deficiencies. Platelet function defects were defined as defects in platelet aggregation and/or platelet ATP release with 1 or more agonists. VWD was defined as von Willebrand factor antigen (VWF:Ag) and/or von Willebrand ristocetin cofactor (VWF:RCo) < 50%.

Analysis

For each symptom, sensitivity, specificity, positive and negative predictive values for a hemostatic disorder were calculated using a 2 × 2 table. The symptoms that showed high predictive values were combined in different “and” “or” combinations and used as a single variable to calculate sensitivity, specificity, and positive and negative predictive values. All the analyses were done using SAS statistical package (version 9.1, SAS Institute, Cary, NC).

Results

One hundred forty-six women between the ages of 13 and 53 years with a physician diagnosis of menorrhagia were enrolled in the study. Characteristics of the study population are shown in Table 1. On laboratory testing, 70% of the participants (102/146) were found to have 1 or more hemostatic abnormalities, including platelet aggregation abnormalities, platelet ATP release defects, decreased von Willebrand factor, or coagulation factor deficiencies. Platelet function defects were present in 67% (98/146) of women, including 30% (44/146) with both platelet aggregation and ATP release defects, 11% (16/146) with platelet aggregation defects and 26% (38/146) with platelet ATP release abnormalities. Seven percent (10/146) had coagulation factor deficiencies including deficiencies of Factors VII, V, and XI and 8% (12/146) of women had VWD based on laboratory testing.

TABLE 1.

Demographic characteristics of study participants (n = 146)

	N (%)	Mean ± SD	Range
Age (y)		33.8 ± 12.4	13-53
Race			

White	104 (71)		
Black	28 (19)		
Other	14 (10)		
Blood group			
O	76 (52)		
Non-O	70 (48)		
Hemoglobin (g/dL)		11.9 ± 2.1	4-15.4
Pictorial blood loss assessment[a]	N = 104	275.8 ± 261.5	24-2036
Score >100	85 (82)	323 ± 267	102-2036
Score >185	62 (60)	389 ± 285	190-2036

Philipp. A screening tool for women with menorrhagia. Am J Obstet Gynecol 2008.
[a] Based on available PBAC information.

The response rate for individual symptoms which were not contingent on positive responses to previous questions ranged from 85-99%. The proportion of women with menorrhagia reporting symptoms related to the severity of bleeding ranged from 47-86% for the individual symptoms (Table 2). More than half the study population reported symptoms, including a menstrual duration of more than 7 days, flooding, bleeding through pads or tampons, or the perception that they had more bleeding compared to other women. Spontaneous bleeding symptoms were reported in 18-65% of women, with easy bruising being the most commonly reported spontaneous bleeding symptom in the study population (65%) (Table 2). Among contingency questions, 17% of women reported excessive bleeding with teeth extraction, 21% reported excessive bleeding with surgical procedures, and 30% of women reported excessive bleeding following childbirth. Ninety percent of women reporting a history of anemia were previously treated for their anemia (Table 2).

TABLE 2.

Percent subjects with A, bleeding symptoms, and B, sensitivity, C, specificity, D, positive predictive value (PPV), and E, negative predictive value (NPV) of bleeding symptoms for bleeding disorders

	A	**B**	**C**	**D**	**E**
Symptoms	**% Positive**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**

	(#positive/Total)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
Menstrual symptoms					
Duration of menses > 7 days	60 (84/140)	62 (53-72)	45 (30-60)	73 (63-82)	34 (22-46)
Bleeding through pads or tampons	72 (104/144)	70 (61-79)	22 (10-34)	66 (57-75)	25 (12-38)
Flooding	77 (111/145)	78 (70-86)	27 (14-40)	70 (62-79)	35 (19-51)
Restricted daily activities	47 (68/145)	47 (37-57)	53 (39-68)	69 (58-80)	31 (21-41)
Bleeding compared to others	86 (108/126)	87 (80-94)	18 (6-30)	70 (62-79)	39 (16-61)
Spontaneous bleeding symptoms					
Nose bleed > 20 lifetime episodes	18 (26/142)	16 (9-24)	78 (66-90)	62 (43-80)	30 (22-39)
Nose bleed as child (> 1/month)	37 (53/142)	38 (28-48)	64 (50-78)	70 (57-82)	33 (23-42)
Easy bruising	65 (83/127)	59 (49-69)	21 (9-36)	63 (52-73)	18 (7-30)
Bruising (> 1/wk)	26 (37/141)	23 (14-31)	66 (52-80)	59 (44-75)	28 (19-37)
Bleeding from lips, tongue, or gums	29 (35/120)	29 (19-39)	71 (57-85)	69 (53-84)	32 (22-42)
Bleeding from cuts	18 (17/94)	17 (8-26)	79 (63-94)	65 (42-87)	29 (18-39)
Excessive bleeding after challenge					
After tooth extraction[a]	18 (20/109)	15 (7-23)	72 (56-89)	60 (39-81)	24 (15-32)
After surgery[a]	21 (18/87)	17 (8-27)	72 (56-89)	56 (33-79)	30 (20-41)
After delivery or miscarriage[a]	30 (24/80)	26 (14-38)	62 (43-80)	58 (39-78)	29 (17-40)
After any challenge[a]	33 (44/132)	28 (19-37)	55 (40-70)	59 (45-74)	25 (16-34)
Anemia and management of bleeding					
Medical treatment to stop bleeding	8 (12/144)	9 (3-15)	93 (86-100)	75 (51-100)	31 (23-39)
Dilatation & curettage	33 (48/145)	31 (22-40)	62 (48-76)	65 (51-78)	29 (20-38)
History of anemia	58 (83/142)	61 (52-71)	48 (33-62)	72 (63-82)	36 (23-48)
Treatment of anemia[a]	90 (74/82)	93 (87-100)	18 (2-34)	76 (66-85)	50 (15-85)
Family history					
Menorrhagia in mother	70 (65/93)	66 (54-78)	23 (8-37)	63 (51-75)	25 (9-41)

Menorrhagia in sister/s[a]	50 (37/74)	51 (37-65)	52 (32-72)	68 (52-83)	35 (20-51)
Bleeding symptoms	32 (37/114)	26 (16-36)	55 (39-71)	54 (38-70)	27 (17-37)
Bleeding disorder	17 (22/133)	13 (6-20)	76 (62-89)	55 (34-75)	28 (20-36)
PBAC score					
Score > 100	82 (85/104)	80 (71-89)	14 (1-27)	72 (62-81)	21 (3-39)
Score > 185	60 (62/104)	55 (44-66)	29 (12-45)	68 (56-79)	19 (7-31)
PFA-100	15 (13/86)	21 (10-31)	96 (90-100)	92 (78-100)	37 (26-48)

Philipp. A screening tool for women with menorrhagia. Am J Obstet Gynecol 2008.
[a] Contingent question.

The sensitivity of individual bleeding symptoms for bleeding disorders ranged from 9% ("medical treatment to stop bleeding") to 86% ("more bleeding compared to others") for noncontingent questions, and from 15% ("excessive bleeding after tooth extraction") to 93% ("treatment of anemia") for contingent questions (Table 2).

Different combinations of bleeding symptoms in women with menorrhagia were analyzed and a set of questions was selected for the screening tool in order to maximize the sensitivity and minimize the number of women with abnormal hemostatic testing missed by the screening tool. Since the screening tool was not intended to be diagnostic for bleeding disorders, but rather designed to stratify women for comprehensive hemostatic testing, a high sensitivity of the screening tool rather than specificity was preferred. Based on the combination of questions giving the highest sensitivity, a screening tool instrument was developed (Table 3). Eight questions were included in the screening tool: 1) duration of periods; 2) history of flooding; or 3) restriction of daily activities during periods; 4) diagnosis of bleeding disorder in family; 5) history of bleeding after tooth extraction; 6) history of bleeding after surgery; 7) history of bleeding after delivery or miscarriage; 8) history of treatment of anemia (Table 3). A combination of 8 questions in 4 categories resulted in the highest sensitivity. Therefore, a screening tool was considered to be positive if 1 of the following 4 criteria were met: 1) the duration of menses was greater than or equal to 7 days and the woman reported either "flooding" or impairment of daily activities with most periods; 2) a history of treatment of anemia; 3) a family history of a diagnosed bleeding disorder; or 4) a history of excessive bleeding with tooth extraction, delivery or miscarriage, or surgery.

TABLE 3.

Proposed screening tool for women with menorrhagia

Q1. How many days did your period usually last, from the time bleeding began until it completely stopped	
i. Less than 7 days	00

ii. Greater than or equal to 7 days	01
iii. Don’t know	88
Q2. How often did you experience a sensation of “flooding” or “gushing” during your period	
i. Never, rarely, or some periods	00
ii. Every or most periods	01
iii. Don’t know	88
Q3. How often your periods limit your daily activities such as work, housework, exercise, or social activities	
i. Never, rarely, or some periods	00
ii. Every or most periods	01
iii. Don’t know	88
Q4. Have you ever been treated for anemia	
i. No	00
ii. Yes	01
iii. Don’t know	88
Q5. Has anyone in your family ever been diagnosed with a bleeding disorder	
i. No	00
ii. Yes	01
iii. Don’t know	88
Q6. Have you ever had a tooth extracted or had dental surgery	
i. No (If no go to Q7)	00
ii. Yes	01
iii. Don’t know	88
Q6a. Did you have problem with bleeding after tooth extraction or dental surgery	
i. No	00
ii. Yes	01
iii. Don’t know	88

Q7. Have you ever had surgery other than dental surgery	
i. No (If no go to Q8)	00
ii. Yes	01
iii. Don't know	88
Q7a. Did you have bleeding problem after surgery	
i. No	00
ii. Yes	01
iii. Don't know	88
Q8. Have you ever been pregnant	
i. No	00
ii. Yes	01
iii. Don't know	88
Q8a. Have you ever had bleeding problem following delivery or after a miscarriage	
i. No	00
ii. Yes	01
iii. Don't know	88

Philipp. A screening tool for women with menorrhagia. Am J Obstet Gynecol 2008.

A positive screening tool had a sensitivity of 82% for hemostatic disorders (including platelet function defects, VWD, or coagulation factor deficiency) and also for VWD and platelet function defects when analyzed separately (Table 4). Adding the performance of the PFA-100 to the screening tool did not improve the sensitivity for bleeding disorders overall, though sensitivity for VWD was increased (Table 4). However, combining the results of the PBAC score (positive > 100) with the screening tool increased the sensitivity to 94% for hemostatic disorders with similar increases in sensitivity for VWD and platelet function defects individually (Table 4). Subanalyzing adolescents (≤ 19 years) (38 subjects) and adults (20-44 years [78 subjects] and ≥ 45 years [30 subjects]) separately did not significantly change the sensitivity of the combined screening tool with PBAC score for bleeding disorders (sensitivity 92%, 95%, respectively). However, there were age differences observed when the screening tool without the PBAC was evaluated. Sensitivity for bleeding disorders was highest (93%) in women 20-44 years old, intermediate in women ≥ 45 years old (81%), and lowest in adolescents (62%). Adding the performance of the PFA-100 to the screening tool and the PBAC did not result in a further

increase in sensitivity. Specificity was low for the screening tool and remained low with the addition of the PBAC score and the PFA-100 (Table 4).

TABLE 4.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for screening tool and screening tool combined with PBAC > 100 and PFA-100

	Sensitivity %	**Specificity %**	**PPV %**	**NPV %**
	(95% CI)	**(95% CI)**	**(95% CI)**	**(95% CI)**
Screening tool[a]				
Bleeding disorder[b]	82 (75-90)	24 (12-37)	71 (63-79)	38 (20-56)
VWD[c]	83 (62-100)	20 (13-27)	9 (3-14)	93 (84-100)
Platelet function defects	84 (76-91)	27 (15-40)	70 (62-78)	45 (27-63)
Screening tool[a] combined with PFA-100				
Bleeding disorder[b]	84 (77-91)	24 (12-37)	71 (63-80)	41 (22-59)
VWD[c]	92 (76-100)	19 (13-26)	9 (4-14)	96 (89-100)
Platelet function defects	85 (78-92)	25 (13-37)	70 (61-78)	44 (26-63)
Screening tool[a] combined with PBAC score > 100				
Bleeding disorder[b]	94 (89-99)	16 (5-26)	71 (64-79)	54 (27-81)
VWD[c]	92 (76-100)	9 (4-14)	8 (4-13)	92 (78-100)
Platelet function defects	94 (89-99)	15 (5-25)	69 (61-77)	54 (27-81)
Screening tool[a] combined with PBAC score > 100 and PFA-100				
Bleeding disorder[b]	95 (91-99)	16 (5-26)	72 (64-79)	58 (30-86)
VWD[c]	92 (76-100)	8 (4-13)	8 (4-13)	92 (76-100)
Platelet function defects	95 (91-99)	15 (5-25)	69 (62-77)	58 (30-86)

Philipp. A screening tool for women with menorrhagia. Am J Obstet Gynecol 2008.

[a] Positive screening tool—see Results section.

[b] Platelet function defects or coagulation factor deficiency or low VWF.

[c] VWFAg or RistCo < 50%.

The effectiveness of the screening tool was also assessed by determining how many females who had an underlying hemostatic disorder would have been missed using the screening tool. Using the screening tool alone, 12% (18/146) of menorrhagia subjects would not have undergone testing and yet had an underlying hemostatic disorder; 82% (83/101) of those with a bleeding disorder would have been found using the screening tool to stratify women for testing. When performance of the PBAC was added to the screening tool, 4% (6/146) of menorrhagia subjects would not have undergone testing and yet had abnormal hemostatic testing and 94% (95/101) of those with an underlying hemostatic disorder would have been found. The results were similar when performance of the PFA-100 was added to performance of the PBAC and the screening tool for stratifying women (3% of menorrhagia women missed and 95% of those with bleeding disorders found). When VWD was analyzed separately, only 1.4% (2/146) of the menorrhagia population would have been missed using the screening tool and 83% of women with VWD were found using the screening tool. When performance of the PBAC was added to the screening tool, 92% of those with VWD would have been found. These results were no different if performance of the PFA-100 was added to the PBAC and the screening tool.

Comment

This study demonstrates the feasibility of a short 8 question screening instrument to stratify women with menorrhagia for hemostatic testing and evaluation. The addition of the PBAC to the screening questionnaire further increased the sensitivity. It is noteworthy that the PFA-100, a potential laboratory screening test, did not add to the sensitivity of the screening tool and PBAC. From the public health perspective, the absence of the need to incorporate laboratory testing into a screening algorithm would make adoption of a screening algorithm in routine gynecology clinical practice more feasible. Based on the results of the present study, however, optimization of the sensitivity of the screening algorithm would require institution into clinical practice of the PBAC, a measurement of menstrual flow based on patient's assessed pad/tampon saturation and count, which is currently seldom used outside of clinical studies.[21] Our results lend support to the incorporation of the PBAC or other validated measurements of menstrual flow in routine clinical practice.

The severity of menstrual bleeding, as demonstrated by the PBAC, duration of menses greater than 7 days, and flooding or impairment of daily activities, appears to be an important criterion for screening women for hemostatic testing. Although the objective definition of menorrhagia has been menstrual blood loss in excess of 80 mL, studies have demonstrated that fewer than half the women diagnosed with menorrhagia and referred for clinical studies meet volume based menstrual blood loss criterion.[22] and [23] Warner et al reported that among routine menorrhagia patients only 38% had a menstrual loss measurement of > 80 mL[21] and referral by a family physician for menorrhagia was not predictive of higher menstrual blood loss.[24] The data from the present study suggest that women diagnosed with menorrhagia who have symptoms of heavier menstrual blood loss, as identified in the screening tool and/or PBAC, may represent a subgroup within the general menorrhagia population more likely to have a bleeding disorder.

To date, a screening questionnaire in women with menorrhagia useful for hemostatic disorders has not been reported. Sramek et al in a study involving subjects with a proven bleeding disorder compared to healthy controls found, similarly to the present study, that diagnosed bleeding disorders in family members and bleeding with traumatic events had high discriminatory

power.[25] The present study, besides the different target population, however, was prospective with the diagnosis of bleeding disorders performed after questionnaire administration and PBAC completion, reducing potential recall bias. More recently, a bleeding score has been proposed to assess the severity of bleeding symptoms in subjects with VWD type 1 compared to controls.[26] Based on an extensive questionnaire, having 3 or more symptoms resulted in a high specificity (99.5%) but low sensitivity (50%), while cutaneous bleeding and post tooth extraction was the best predictor of type 1 VWD.[26] The applicability of the bleeding score for screening the menorrhagia population and for other hemostatic disorders besides VWD has not been reported. The high specificity with modest sensitivity lends credence to the suggestion that the primary benefit of the bleeding score may be in the hematology setting for incorporation into the optimal diagnosis of Type 1 VWD as has been proposed,[27] rather than incorporation into a screening algorithm for primary care practice. In addition, the bleeding score may be a useful measure of bleeding risk or severity although it has not been validated with platelet function defects. In contrast, the low specificity with high sensitivity of the present screening tool limits its usefulness to initial screening, rather than to the definitive diagnosis, in conjunction with comprehensive laboratory testing of bleeding disorders.

We conclude, based on the present data, that a short questionnaire based screening tool may be useful in targeting which women with unexplained menorrhagia and potential undiagnosed bleeding disorders warrant consideration for comprehensive hemostatic testing and evaluation. Further multi-institutional studies in discrete gynecologic subpopulations, including adolescents, prospectively validating the benefits of incorporating the screening tool in routine gynecologic practice are warranted.

References

1 A. Dilley, C. Drews and C. Miller *et al.*, Von Willebrand disease and other inherited bleeding disorders I women with diagnosed menorrohagia, *Obstet Gynecol* **97** (2001), pp. 630–636. SummaryPlus | **Full Text + Links** | PDF (187 K) | View Record in Scopus | Cited By in Scopus (71)

2 R.A. Kadir, D.L. Economides, C.A. Sabin, D. Owens and C.A. Lee, Frequency of inherited bleeding disorders in women with menorrhagia, *Lancet* **351** (1998), pp. 485–489. SummaryPlus | **Full Text + Links** | PDF (71 K) | View Record in Scopus | Cited By in Scopus (151)

3 M. Edlund, M. Blomback, B. von Schoultz and O. Andersson, On the value of menorrhagia as a predictor for coagulation disorders, *Am J Hematol* **53** (1996), pp. 234–238. **Full Text** via CrossRef | View Record in Scopus | Cited By in Scopus (80)

4 C.S. Philipp, A. Faiz and N. Dowling *et al.*, Age and the prevalence of bleeding disorders in women with menorrhagia, *Obstet Gynecol* **105** (2005), pp. 61–66.

5 A.H. James, A.S. Lukes, L.R. Brancazio, E. Thames and T.L. Ortel, Use of a new platelet function analyzer to detect von Willebrand disease in women with menorrhagia, *Am J Obstet Gynecol* **191** (2004), pp. 449–455. SummaryPlus | **Full Text + Links** | PDF (179 K) | View Record in Scopus | Cited By in Scopus (16)

6 M. Shankar, C.A. Lee, C.A. Sabin, D.L. Economides and R.A. Kadir, Von Willebrand disease in women with menorrhagia: a systematic review, *BJOG* **11** (2004), pp. 734–740. **Full Text** via CrossRef | View Record in Scopus | Cited By in Scopus (26)

7 C.S. Philipp, A. Dilley and C.H. Miller *et al.*, Platelet functional defects in women with unexplained menorrhagia, *J Thromb Haemost* **1** (2003), pp. 477–484. **Full Text** via CrossRef | View Record in Scopus | Cited By in Scopus (30)

8 J. Bevan, K. Maloney, C. Hillery, J. Gill, R. Montgomery and S. Paul, Bleeding disorders: a common cause of menorrhagia in adolescents, *J Pediatr* **138** (2001), pp. 856–861. Abstract | PDF (71 K) | View Record in Scopus | Cited By in Scopus (37)

9 R. Saxena, M. Gupta, P. Gupta, R. Kashyap, V. Choudhry and M. Bhargava, Inherited bleeding disorders in Indian women with menorrhagia, *Hemophilia* **9** (2003), pp. 193–196. **Full Text** via CrossRef | View Record in Scopus | Cited By in Scopus (12)

10 F. Rodeghiero, G. Castaman and E. Dini, Epidemiological investigation of the prevalence of von Willebrand's disease, *Blood* **69** (1987), pp. 454–459. View Record in Scopus | Cited By in Scopus (279)

11 R.A. Lipton, Misdiagnosis by milk box, *Haemophilia* **9** (2003), p. 235. **Full Text** via CrossRef | View Record in Scopus | Cited By in Scopus (5)

12 ACOG Committee Opinion, Menstruation in girls and adolescents: using the menstrual cycle as a vital sign, *Obstet Gynecol* **108** (2006), pp. 1323–1328.

13 Royal College of General Practitioners, Morbidity statistics from general practice 1981-1982, HMSO, London (1986).

14 M. Rees, Menorrhagia, *BMJ (Clin Res Ed)* **294** (1987), pp. 759–762. View Record in Scopus | Cited By in Scopus (27)

15 M.K. Oehler and M.C. Rees, Menorrhagia: an update, *Acta Obstet Gynecol Scand* **82** (2003), pp. 405–422. **Full Text** via CrossRef | View Record in Scopus | Cited By in Scopus (27)

16 N.C. Lee, R.C. Dicker, G.L. Rubin and H.W. Ory, Confirmation of the preoperative diagnoses for hysterectomy, *Am J Obstet Gynecol* **150** (1984), pp. 283–287. View Record in Scopus | Cited By in Scopus (72)

17 C.S. Philipp, C.H. Miller and A. Faiz, Screening women with menorrhagia for underlying bleeding disorders: the utility of the platelet function analyzer and bleeding time, *Haemophilia* **11** (2005), pp. 497–503. **Full Text** via CrossRef | View Record in Scopus | Cited By in Scopus (9)

18 J.M. Higham, P.M.S. O'Brien and R.W. Shaw, Assessment of menstrual blood loss using a pictorial chart, *BJOG* **97** (1990), pp. 734–739