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COMMENTARY

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All bleeding matters … but the details may not

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In this issue of *Research and Practice in Thrombosis and Haemostasis*, Spradbrow et al[1] report on the association between individual bleeding symptoms in bleeding assessment tools (BATs) and the likelihood of a diagnosis of von Willebrand Disease (VWD). To examine these relationships, the authors used bleeding scores from 927 subjects 12 to 90 years of age (mean age, 40 years) collected via expert administration prior to a laboratory diagnosis of VWD. These "legacy data" stem from a portfolio of studies completed by this group of investigators, led by Dr Paula James from Queens University, which examine the use of standardized BATs in a variety of patient populations and clinical settings. This particular investigation was motivated, as have been many others over the past decade, by an ongoing quest to streamline and optimize BATs in order to improve their clinical utility. In other words, if we can identify the symptoms that are most predictive of bleeding disorders, can we shorten BATs by only including those questions?

The ability to precisely and objectively quantify bleeding symptoms through the use of BATs has long been of interest to the hematology community. Taking a thorough bleeding history is one of the most essential and frequently utilized skills of a trained hematologist, yet it remains challenging due to the frequency of bleeding symptoms in the general population. In a survey of 500 healthy adults, for example, Mauer et al[2] found that 25% reported epistaxis; almost 20% experienced easy bruising, hematochezia, or bleeding after tooth extraction; and almost one half of females reported heavy menstrual bleeding. Not only are bleeding symptoms common, but the severity of patient-reported symptoms can be over- or underrated due to a variety of factors including patients' personality types, their experience with bleeding in a family member, and the manner in which symptoms are collected (eg, self-administered surveys as compared to a guided interview). Given these challenges, the value of BATs seems clear, and in fact a growing body of literature has demonstrated their ability to discriminate between healthy subjects and those with VWD in both the adult and pediatric populations.[3–5]

Despite their clear utility in the academic and research arenas, however, the ability to implement BATs into clinical practice remains elusive. An illustration of this conundrum is the work by Duran et al[6] in the use of a BAT (the Pediatric Bleeding Questionnaire [PBQ] in this case) to screen for VWD in a primary care setting. In this study, during a 3-month intervention period, 8 clinics conducted screening assessments with the PBQ when evaluating young female patients who had been menstruating for at least 6 months. After the intervention period, the majority of providers reported that the PBQ was an "important" tool of "good" quality that enhanced their clinical abilities "quite a bit" when it came to evaluating bleeding symptoms. And in most cases, the PBQ took only 2 minutes to complete. However, only 101 of 339 young women had a BAT score documented, indicating only 30% provider fidelity to this seemingly simple intervention. In post-study surveys, providers admitted that they often simply forgot to complete the PBQ or felt overwhelmed by more pressing obligations in their clinical practice. Therefore, the question remains: Can we make the BATs easier to administer?

The paper by Spradbrow et al[1] found that the symptom for which a clinically significant positive response most increased the likelihood of VWD was hemarthrosis, which is unfortunately a not-so-helpful finding given the rarity of this symptom outside of type 3 VWD. Also, it seems quite doubtful that a hematologist would choose not to thoroughly evaluate a patient with hemarthrosis for an underlying bleeding disorder regardless of their total BAT score. The other most predictive symptoms were postsurgical bleeding and menorrhagia, certainly more common presenting complaints in consultative hematology. In fact, in their multivariable model, muscle hematoma and central nervous system bleeding were the only symptoms found not to significantly increase the odds of VWD, likely due to their rarity

in both the case and control populations. Since the authors did find that some symptoms have greater predictive value than others, they conclude that future revisions of BATs may benefit from the addition of relative weighting for each symptom and perhaps adjusting these weightings for age and gender. While their suggestion may be mathematically true, I believe that incorporation of such strategies would simply serve to increase the unwieldy nature of these instruments and further decrease their clinical utility.

In my opinion, the most important finding of this paper is that the number of categories of clinically significant bleeding symptoms reported by an individual had a major impact on the odds ratio for a VWD diagnosis, regardless of the severity of the symptom. An individual with 2 bleeding symptoms has a VWD odds ratio 5-fold higher than an individual with 1 bleeding symptom, and an individual with 3 symptoms has an odds ratio 15-fold higher than an individual with 2 symptoms (Figure 1). As the authors note, this finding has also been reported in adults by Rodeghiero et al,[7] who found that having 2 bleeding symptoms, regardless of severity, was useful in discriminating between type 1 VWD patients and healthy controls. While Spradbrow et al chose not to include patients <12 years of age in their analyses due to small sample size, our own group's work in a pediatric population has also shown that the negative predictive value for VWD and platelet function defects was comparably high with qualitative (number of bleeding symptoms) and quantitative (bleeding score) criteria.[8]

I find this "shortcut" particularly intriguing because I will publicly admit in this forum that even I, a hematologist who has investigated, published, and lectured on the utility of BATs for almost a decade, do not formally administer a BAT to the numerous new patients I see each year presenting with symptoms of bruising or bleeding. My excuses likely ring true with other colleagues: "clinic is too busy," "I can't get my fellows to do it," "most of my pediatric/adolescent patients never have many of these symptoms," or "I have to check labs anyway or the referring physician will be offended." Most recently and notably, despite a passionate trainee spending almost a year working with our electronic medical record support team, we still could not achieve the goal of having a patient-completed BAT on an electronic tablet merge into their electronic medical record, and who has time to enter all that information by hand?

The strengths of the legacy data source used by Spradbrow et al[1] are many and include the large patient population, the ability to overlap the various Vicenza-based BATs used in the prior studies, the fact that these BATs were administered by trained investigators (and in many cases the same investigative teams participated in the included studies), and the clear and uniform laboratory definitions of VWD. One notable limitation of the legacy data, however, is that the controls included in these studies were typically healthy subjects responding to advertisements or patients recruited from clinic waiting rooms who answered no to screening questions regarding whether they had experienced problems with bruising or bleeding. These controls are inherently different from the "controls" we see in our hematology clinics, who in most cases have been referred to us precisely because they have experienced problems with bruising or bleeding, but who at the end of our evaluation will turn out not to have an underlying bleeding diathesis.

In the end, I believe that BATs are most useful in the consultative hematology setting. Although I have admitted to not formally administering the full instruments to all of my new patients, I still find the BATs helpful in my practice. BATs have consistently demonstrated a high negative predictive value, so when I am evaluating a patient for whom I really do not believe that additional hematologic evaluation is indicated, I find it helpful (and hopefully reassuring to the referring physician) to state in my letter that one of the reasons I have elected not to pursue initial or additional laboratory testing is that the patient's bleeding score is normal as per a standardized BAT. Likewise, if the bleeding score is clearly high and VWD testing is normal, I know that I need to actively pursue alternate diagnoses, and will likely continue to follow this patient as a "bleeding disorder not otherwise specified"[9] if additional laboratory testing continues to be unremarkable and the patient does not have evidence of a joint hypermobility syndrome.

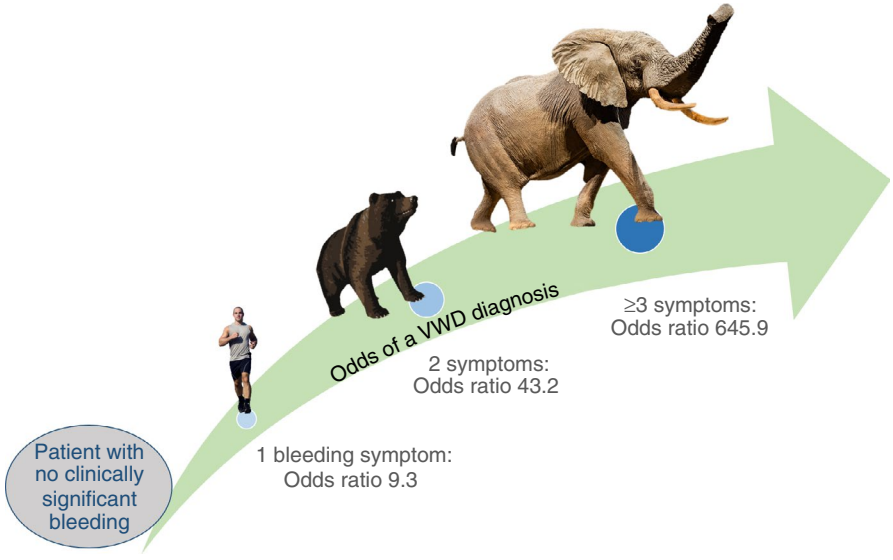

FIGURE 1 As compared to a patient with no clinically significant bleeding symptoms, the odds of a diagnosis of von Willebrand disease (VWD) increase exponentially with each unique bleeding symptom

So while Spradbrow et al[1] have demonstrated that all bleeding does matter and that we, unfortunately, cannot remove questions from BATs to make them more facile tools, they have importantly also shown that the details of such bleeding may not matter. Counting up the number of bleeding symptoms endorsed by a patient is a great start to better identifying patients with inherited bleeding disorders, and this strategy seems much more feasible for a primary care provider, the hematology fellow in training, and even the expert hematologist pressed for time.

RELATIONSHIP DISCLOSURE

The author reports nothing to disclose.

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