Turk J Hematol 2020;37:57-76

Assessment of Patients with von Willebrand Disease with ISTH/BAT and PBQ Scores

Von Willebrand Hastalığı Olgularının ISTH/BAT ve PBQ Skorları ile Değerlendirilmesi

Fatma Burcu Belen Apak[1], Elif Gülsüm Ümit[2], Yağmur Zengin[3], Melike Sezgin Evim[4], Ekrem Ünal[5], Hasan Mücahit Özbaş[6], Can Acıpayam[7]

[1]*Başkent University Faculty of Medicine, Department of Pediatric Hematology Oncology, Ankara, Turkey*
[2]*Trakya University Faculty of Medicine, Department of Hematology, Edirne, Turkey*
[3]*Başkent University Faculty of Medicine, Department of Biostatistics, Ankara, Turkey*
[4]*Uludağ University Faculty of Medicine, Department of Pediatric Hematology Oncology, Bursa, Turkey*
[5]*Erciyes University Faculty of Medicine, Department of Pediatric Hematology Oncology, Kayseri, Turkey*
[6]*Giresun University Faculty of Medicine, Department of Hematology, Giresun, Turkey*
[7]*Kahramanmaraş Sütçü İmam University Faculty of Medicine, Department of Pediatric Hematology and Oncology, Kahramanmaraş, Turkey*

To the Editor,

The Turkish Society of Hematology initiated the Turkish Hemophilia Masterclass Academy program in 2016 to encourage young hematologists entering the field of hemophilia. The program involved 6 months of training, supported by monthly exams. We, as a group of mentees from the Hemophilia Masterclass Academy, aimed to evaluate the bleeding phenotype of patients with von Willebrand Disease (VWD) using the International Society of Thrombosis and Haemostasis-Bleeding Assessment Tool (ISTH-BAT) and the Pediatric Bleeding Questionnaire (PBQ) scores and investigate the correlation of von Willebrand factor antigen (VWF:Ag) levels and bleeding scores of the patients, as well as present the initial output of our Masterclass Academy.

The study included 62 patients (aged 3-61 years) with the diagnosis of VWD (54 patients with VWD type 1 and 8 with VWD type 3). The ISTH-BAT and PBQ were administered to patients who were ≥18 years old and <18 years old, respectively. Informed consent was obtained from all patients.

The VWF:Ag levels, ristocetin cofactor activity (VWF:Ricof), and FVIII levels were retrospectively reviewed from the patient records. The cut-off point for a positive score was accepted as ≥2 for the PBQ and ≥3 for the ISTH-BAT. Statistical analysis was performed using SPSS 17.0. Demographic findings, median bleeding scores, and VWF levels are presented in Table 1. Epistaxis, superficial bleedings, bleeding from minor wounds, oral bleeding, umbilical bleeding, and muscle hematoma were found to be statistically significant in showing dependence between the diagnostic status and the bleeding symptoms ($p<0.05$). The study aimed to investigate the correlation between the VWF:Ag levels and the bleeding scores in our patients. Our study showed that VWF:Ag levels were inversely correlated with the bleeding scores of the patients (Table 2).

The evaluation of bleeding scores dates back to the Vicenza score that was used in VWD patients [1,2,3]. In 2009, Bowman et al. [4] published the PBQ, and it was investigated in our population with VWD previously [5]. In 2010, the ISTH-BAT score was established by the ISTH/SSC Joint Working Group [6,7]. One of the limitations of our study was the use of the PBQ in children and ISTH-BAT in adults, which might have caused heterogeneity in the evaluation of the scores. Moreover, the lack of a control group, consisting of patients who had bleeding symptoms but were normal by hemostatic tests, left us unable to compare the VWD patients and normal individuals. Although the median total scores of the types 1 and 3 VWD groups were compatible with previous studies, the positive scores reported in each subgroup for epistaxis, oral cavity bleeding, cutaneous bleeding, and bleeding after minor wounds were found to

Table 1. Characteristics of von Willebrand type 1 and type 3 patients.

	VWD type 1 (n=54)	VWD type 3 (n=8)
Median age, years (minimum-maximum)	28 (3-61)	17 (6-30)
Pediatric/Adult	13/41	3/5
Female	46	6
Male	8	2
VWF:Ag (IU/dL)	22.23 (2-50)	2.5 (0-10)
VWF:Ricof (IU/dL)	23.3 (8.3-45)	7.5 (6-23)
FVIII (IU/dL)	45 (15-70)	3 (1-11.5)
Median total score (minimum-maximum)	3 (0-19)	16 (9-27)

VWF:Ag: von Willebrand factor antigen level, VWF:Ricoll: von Willebrand Factor ristocetin cofactor level, VWD: von Willebrand disease.

Table 2. Bleeding scores positivity regarding each symptom in von Willebrand type 1 and type 3 patients.

Bleeding symptom	VWD type 1§	VWD type 3*	p
Epistaxis	22%	100%	**0.000**
Cutaneous bleeding	3.7%	62.5%	**0.000**
Minor bleeding	5.6%	75%	**0.000**
Oral cavity bleeding	5.6%	75%	**0.000**
Bleeding after tooth extraction	22.2%	37.5%	0.295
Intramuscular bleeding	**3.7%**	**37.5%**	**0.013**
Hemarthrosis	3.7%	25%	0.077
Menorrhagia**	41.3%	50%	0.506
Central nervous system bleeding	1.9%	12.5%	0.243
Umbilical bleeding	1.9%	25%	0.041
Postsurgical bleeding	1.7%	0%	0.757
Cephalhematoma	0%	12.5%	0.129
Macroscopic hematuria	3.7%	12.5%	0.344

§ von Willebrand type 1 group (n=54). * von Willebrand type 3 group (n=8).

Epistaxis, superficial bleedings, bleeding from minor wounds, oral bleeding, umbilical bleeding, muscle hematoma, and hemarthrosis were found to be statistically significant in showing dependence between diagnosis status (VWD types 1-3) and bleeding symptoms ($p<0.05$).

**Menorrhagia symptom was compared among female patients in both groups.

VWD: von Willebrand disease

be lower compared to those in the previous literature [4,5,8]. This may be explained by the inclusion of "low VWF levels" (intermediate levels of VWF:Ag, 30-50 IU/dL) in the group with type 1 VWD. People with "low VWF levels" falsely labeled as "VWD type 1 patients" may have lower reported bleeding scores compared to true VWD patients, leading to low positive scores. Our study shows that the ISTH/BAT and PBQ can be useful in the evaluation of the bleeding symptoms of patients. Further studies with larger patient and control groups are warranted to show the usage of bleeding scores in daily outpatient practice. We, as the mentees of the Hemophilia Masterclass, feel much appreciation to our mentors and the Turkish Society of Hematology for their contributions to our progress in the field of hemophilia.

Keywords: Von Willebrand Disease, Pediatric Bleeding Questionnaire, ISTH/BAT score

Anahtar Sözcükler: Von Willebrand Hastalığı, Pediatrik Kanama Skoru, ISTH/BAT skoru

Informed Consent: Informed consent was obtained from all patients or their legal guardians.

Authorship Contributions

Surgical and Medical Practices: F.B.B.A., E.G.Ü., Y.Z., M.S.E., E.Ü., H.M.Ö., C.A.; Concept: F.B.B.A.; Design: F.B.B.A., E.G.Ü; Data Collection or Processing: F.B.B.A., Y.Z.; Analysis or Interpretation: Y.Z., F.B.B.A., E.G.Ü; Literature Search: F.B.B.A., E.G.Ü; Writing: F.B.B.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Tosetto A, Castaman G, Rodeghiero F. Bleeding scores in inherited bleeding disorders: clinical or research tools? Haemophilia 2008:14:415-422.
2. Rodeghiero F, Castaman G, Tosetto A, Batlle J, Baudo F, Cappeletti A, Casana P, De Bosch N, Eikenboom JC, Federici AB, Lethagen S, Linari S, Srivastava A. The discriminant power of bleeding history for the diagnosis of type 1 von Willebrand disease: results from a multicenter study. J Thromb Haemoast 2005;3:2619-2626.
3. Tosetto A, Rodeghiero F, Castaman G, Goodeve A, Federici AB, Batlle J, Meyer D, Fressinaud E, Mazurier C, Goudemand J, Eikenboom J, Schneppenheim R, Budde U, Ingerslev J, Vorlova Z, Habart D, Holmberg L, Lethagen S, Pasi J, Hill F, Peake I. A quantitative analysis of bleeding symptoms in type 1 von Willebrand disease: results from a multicenter European study (MCMDM-1 VWD). J Thromb Haemost 2006;4:766-773.
4. Bowman M, Riddel J, Rand ML, Tosetto A, Silva M, James PD. Evaluation of the diagnostic utility for von Willebrand disease of a pediatric bleeding questionnaire. J Thromb Haemost 2009;7:1418-1421.
5. Belen B, Kocak U, Isik M, Keskin EY, Oner N, Sal E, Kaya Z, Yenicesu I, Gursel T. Evaluation of Pediatric Bleeding Questionnaire in Turkish children with von Willebrand disease and Platelet function disorders. Clin Appl Thromb Hemost 2015;21:565-569.
6. Rodeghiero F, Tosetto A, Abshire T, Arnold DM, Coller B, James P, Neunert C, Lillicrap D; ISTH/SSC Joint VWF and Perinatal/Pediatric Hemostasis Subcommittees Working Group. ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders. J Thromb Haemost 2010;8:2063-2065.
7. Bidlingmaier C, Grote V, Budde U, Olivieri M, Kurnik K. Prospective evaluation of pediatric bleeding questionnaire and the ISTH bleeding assessment tool in children and parents in clinical routine. J Thromb Haemost 2012;10:1335-1341.
8. Pathare A, Omrani SA, Al Hajri F, Al Obaidani N, Al Balushi B, Al Falahi K. Bleeding score in type 1 von Willebrand disease patients using the ISTH-BAT questionnaire. Int J Lab Hematol 2018;40:175-180.

Address for Correspondence/Yazışma Adresi: Fatma Burcu Belen Apak, M.D., Başkent University Faculty of Medicine, Department of Pediatric Hematology Oncology, Ankara, Turkey
Phone : +90 532 581 45 51
E-mail : draidabb@gmail.com ORCID: orcid.org/0000-0002-9278-6703

Received/Geliş tarihi: July 25, 2019
Accepted/Kabul tarihi: November 12, 2019
DOI: 10.4274/tjh.galenos.2019.2019.0446