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ORIGINAL ARTICLE

Joint surgery in von Willebrand disease: a multicentre cross-sectional study

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Background: Joint bleeds are reported by 23% of von Willebrand disease (VWD) patients and associated with orthopaedic surgery. Limited data are available on joint surgery in VWD. **Aim:** To assess the prevalence, indications, management and complications of joint surgery in VWD patients. **Methods:** 804 VWD patients with historically lowest von Willebrand factor (VWF) activity ≤30 U dL^{-1} completed a questionnaire on joint bleeds, joint damage and orthopaedic surgery. We retrieved additional medical file data of patients who underwent surgery on large joints (shoulder, elbow, hip, knee or ankle). **Results:** 116 out of 804 patients (14%) reported large joint surgery. Compared to VWD patients without previous orthopaedic surgery, these 116 patients reported more frequently a history of joint bleeds and joint damage (41% vs. 20%, $P < 0.001$ and 61% vs. 20%, $P < 0.001$). Medical file data on 126 large joint surgeries in 79 VWD patients revealed that this surgery was associated with joint damage due to prior joint bleeds in 24% of the procedures. Preoperative clotting factor correction (CFC) to prevent bleeding was administered in most cases (81%). Documentation on postoperative bleeding was found in 23 surgeries (18%). **Conclusions:** Large joint surgery is reported by 14% of VWD patients, related to joint bleeds in 24% and seems associated with bleeding complications frequently despite perioperative CFC.

Keywords: arthropathy, joint bleeds, orthopaedic surgery, von Willebrand disease

Introduction

von Willebrand disease (VWD) is a heterogeneous inherited bleeding disorder that is characterized by a deficiency of von Willebrand factor (VWF) in type 1 VWD. In type 2 VWD, there is a functional VWF defect and in the most severe type 3 VWD variant, a complete lack of VWF [1]. In more severe VWD, clotting factor VIII (FVIII) can be concomitantly deficient resulting in a more severe bleeding phenotype including joint bleeds [2]. Joint bleeds can result in structural joint damage which may be an indication for joint surgery [3]. Orthopaedic surgery might carry a higher risk of bleeding in patients with a coagulation disorder and joint deformities due to prior bleeds.

The Willebrand in the Netherlands study (WiN) is a nationwide cross-sectional multicentre study in moderate and severe VWD patients in which the study population completed an extensive questionnaire on bleeding symptoms, treatment and quality of life [4].

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Almost a quarter of the 804 VWD patients (self) reported a history of joint bleeds. We previously showed that these joint bleeds have significant impact on health-related quality of life and on joint integrity and that the joint bleeds are also associated with joint surgery [5,6]. However, details on these orthopaedic procedures have not been reported before in the WiN study population.

Although the occurrence of joint bleeds and subsequent joint damage has been recognized in VWD, there is a paucity of data on orthopaedic surgery in VWD patients. This does not only apply to surgery regarding VWD-associated haemophilia-like arthropathy, but also to orthopaedic surgery in VWD patients in general [3,6,7]. The aim of this study is to investigate the prevalence, indications, management and complications of surgery on large joints in VWD patients from the WiN cohort.

Methods

In the WiN-study, VWD patients completed a comprehensive questionnaire between October 2007 and October 2009, including questions on joint bleeds, joint damage and orthopaedic surgery. Patients were eligible if they had bleeding symptoms or a family history of VWD and historically lowest levels of VWF: Antigen level (VWF:Ag) or VWF ristocetin cofactor activity $\leq$30 U dL^{-1} or FVIII concentration (FVIII:C) $\leq$40 U dL^{-1} [4]. Central measurements of VWF:Ag, VWF collagen-binding activity, VWF activity (VWF: Act), FVIII:C and multimer analysis were performed, as has been described before [2,8]. Besides bleeding symptoms including joint bleeds, the questionnaire included questions on treatment of VWD, comorbidity and whether no, mild, moderate or severe permanent impairment of joint function after bleeding had occurred (joint damage) and assessment of the Tossetto bleeding score. Participants were asked about joint surgery with subsequent hospital admission, and details on which joint was involved. In addition, details of up to four surgical procedures were asked, including questions on bleeding during or after the procedure. We analysed these self-reported data focussing on the patients who reported large joint surgery. We defined large joint surgery as any surgical orthopaedic procedure on the ankle, knee, hip, elbow or shoulder.

To investigate the indications, management and complications of orthopaedic surgery, we searched for medical file data on orthopaedic surgery of the WiN patients who reported large joint surgeries in all 13 Dutch haemophilia treatment centres (HTCs). If the surgery had been performed in a non-HTC, we tried to retrieve correspondence on the orthopaedic surgery from that hospital. All patients with medical information on large joint surgeries were included in the analyses. We obtained data on the number, dates, types, locations of and indications for orthopaedic joint surgery. We recorded details on any treatment to correct coagulation factor levels (by means of clotting factor replacement therapy or the administration of desmopressin) and on complications.

Statistical analyses

All available data were analysed; we did not apply any imputation methods for missing data. For statistical analyses, the IBM SPSS Statistics version 21 (IBM Corp., Armonk, NY, USA) was used. Continuous outcome measures were tested for normal distribution with Q-Q plots. Logistic regression with correction for subject number was used to address potential dependency of multiple surgeries within the same patients. Depending on the expected cell counts we used chi square or Fisher's exact test to compare proportions. The independent *t*-test was performed to compare means of continuous variables. Non-parametric Mann–Whitney *U* testing was used for the non-normally distributed continuous data. A *P* value <0.05 was considered statistically significant.

Results

Fourteen percent of the patients in the WiN-study (116/804) reported large joint surgery. Medical file data on orthopaedic surgeries were available in 79 patients. Their baseline characteristics are summarized in Table 1, next to the baseline characteristics of the whole WiN cohort. The median age of all WiN participants at inclusion was 41 years. For the orthopaedic surgery patients, the median age was 59 years. The proportion of type 3 VWD was higher in the joint surgery patients compared to the whole WiN cohort (14% vs. 6%). Coagulation factor levels were similar in the WiN cohort and the joint surgery patients (Table 1).

The 116 VWD patients who reported joint surgery in the WiN-study denoted a history of joint bleeds and joint damage more often compared to the VWD patients not reporting joint surgery (41% vs. 20%, $P < 0.001$ and 61% vs. 20%, $P < 0.001$, respectively). Relevant comorbidity, such as osteoarthritis, occurred more often in the joint surgery patients (15% vs. 6%, $P = 0.001$) (Table 2). Bleeding during or after orthopaedic surgery was reported in the questionnaire by 35% of the joint surgery patients. A history of both joint bleeds and joint damage in the operated joint was reported by 38% (33/86, Table 2).

We were able to obtain medical file data on 126 large joint surgeries, performed between 1982 and 2013, in 79 patients. These procedures included mostly knee surgery (47%), followed by ankle (19%) and hip (18%) surgery (Table 3). Prescriptions of pain medication for joint-related pain were found in 32%

Table 1. Baseline characteristics of the study population.

	WiN cohort (n = 804)	Joint surgery patients (n = 79)
Sex		
Males (n, %)	323 (40)	28 (35)
Females (n, %)	481 (60)	51 (65)
Age (year) at time of WiN		
All (median, range)	41 (0–85)	55 (2–83)
Males (median, range)	36 (0–85)	55 (2–72)
Females (median, range)	44 (0–83)	55 (17–83)
Blood group*		
Blood group O (%)	434 (61)	50 (67)
Type VWD†		
1 (n, %)	454 (57)	45 (57)
2 (n, %)	301 (37)	23 (29)
2A (n)	202	14
2B (n)	55	4
2M (n)	30	2
2N (n)	15	3
3 (n, %)	46 (6)	11 (14)
New centrally measured levels‡		
VWF:Ag (IU dL^{-1}; median, IQR)	29 (18–45)	35 (22–48)
VWF:CB (IU dL^{-1}; median, IQR)	23 (7–51)	27 (7–56)
VWF:Act (IU dL^{-1}; median, IQR)	23 (8–53)	25 (1–55)
FVIII:C (IU dL^{-1}; median, IQR)	51 (33–73)	52 (34–84)

n = 804: whole WiN study population; n = 79: VWD patients with available medical file data on large joint surgery.
WiN, Willebrand in the Netherlands study; VWD, von Willebrand disease; IQR, 25–75% inter quartile range; VWF:Ag, von Willebrand factor antigen level; VWF:CB, VWF collagen binding activity; VWF:Act, VWF activity level; VWF:RCo, VWF ristocetin cofactor binding activity; FVIII:C, factor VIII level.
*n = 715 based on availability.
†Based on centrally determined (n = 649) or historic VWD type (n = 154, type known in the haemophilia treatment centre, 1 missing).
‡n = 630, based on patients of whom plasma was available and after exclusion of pregnant patients and those who had received clotting factor concentrate or desmopressin <72 h before the laboratory assessment.

Table 2. Characteristics of VWD patients self-reporting orthopaedic surgery compared to those not reporting orthopaedic surgery.

Data from WiN questionnaire n = 804	Self-reported OS n = 116	No OS reported n = 688	P value
Sex			
Males (n, %)	43 (37)	280 (41)	0.46
Females (n, %)	73 (63)	408 (59)	
Age at WiN incl (year)			
Median (range)	53 (17–78)	39 (0–85)	<0.001
Type VWD*			
1 (n, %)	72 (63)	382 (55)	0.16
2 (n, %)	32 (28)	271 (39)	0.02
3 (n, %)	11 (10)	35 (5)	0.06
Severe VWD†			
VWF:Act ≤ 10 IU dL^{-1} (%)	22 (22)	155 (29)	0.14
FVIII ≤ 10 IU dL^{-1} (%)	8 (8)	25 (5)	0.17
VWF:Act or FVIII ≤ 10 IU dL^{-1} (%)	22 (22)	159 (30)	0.12
Joint bleeds			
Reported in WiN	47 (41)	137 (20)	<0.001
In the same joint as OS	38 (33)	–	–
Knee (n, %)	30 (26)	73 (11)	<0.001
Ankle (n, %)	24 (21)	68 (10)	0.001
Elbow (n, %)	14 (12)	30 (4)	0.001
Shoulder (n, %)	4 (3)	22 (3)	0.89
Hip (n, %)	6 (5)	9 (1)	0.004
Bleeding during or after surgery‡			
Large joint surgery (%)	33/93 (35)	–	
Large joint damage§			
Knee, ankle, elbow, shoulder, hip (%)	71 (61)	138 (20)	<0.001
In the same joint as OS (%)	64/99 (65)	–	–
Both JB&JD in same joint as OS (%)	33/86 (38)	–	–
Comorbidity¶			
Influencing muscle-joint function (%)	17 (15)	41 (6)	0.001

VWF, von Willebrand factor; OS, orthopaedic surgery of large joints (knee, ankle, elbow, shoulder, hip); VWD, von Willebrand disease; JB, joint bleeds; JD, joint damage; incl, inclusion; WiN: Willebrand in the Netherlands study.
*Based on patients of whom plasma was available (n = 649) or historical type VWD (n = 154, 1 missing).
†Based on n = 99 OS patients and n = 531 no OS patients of whom plasma was available and after exclusion of pregnant patients and those who had received clotting factor concentrates or desmopressin <72 h before the laboratory assessment.
‡Based on details of 1–4 operations reported by 615/804 participants.
§Permanent mild, moderate or severe impairment of joint function.
¶Complete list of relevant comorbidity in Table S1.

(25/79) of these patients files. Documentation was found on one large joint operation in most cases (50/79, 63%), on two operations in 19 patients (24%) up to a maximum of 7 orthopaedic interventions in 1 case. Arthroscopic surgery was performed in 44% of the procedures (55/126). Knee surgery was arthroscopic in most cases (43/59, 73%), most commonly partial meniscectomy (22/43, 51%). The majority of orthopaedic surgeries were performed in a HTC (76/126, 60%). Previous joint damage due to joint bleeds was the operation indication in 24% of the surgeries (Table 3). The median age at joint surgery was 45 years (range = 6–77). Joint surgery because of previous joint damage due to joint bleeds was performed at younger age than joint surgery for other indications (median age = 28 year vs. 48 year, $P < 0.001$). Type 3 VWD patients had their first orthopaedic surgery at a younger age compared to non-type 3 VWD patients (mean age = 31 year vs. 47 year, $P = 0.001$).

Preoperative clotting factor correction (CFC) with clotting factor concentrates or desmopressin to prevent bleeding was administered in most surgeries (88/109, 81%, not documented in 17 surgeries, Table 3). Postoperative bleeding was documented in 24% (19/79) of the patients in 18% (23/126) of the orthopaedic procedures. Regarding this bleeding, there was no significant difference between arthroscopic and non-arthroscopic surgery (27% vs. 18%, $P = 0.31$), use of preoperative CFC (bleeding in 15/88 with CFC, 17% vs. 7/21 without CFC, 33%, $P = 0.09$), VWD phenotype (mean bleedings score 16.4 vs. 14.5 in patients with and without a documented postoperative bleed, $P = 0.33$), mean duration of treatment with clotting factor concentrates (6 days vs. 7 days, $P = 0.55$), nor between surgery performed in HTC vs. non-HTC (17% vs. 20%, $P = 0.68$) (Table 4). Postoperative bleeding despite prophylactic CFC occurred in 13 patients (in 15/23 surgeries with documented bleeding complications). These patients did not have type 3 VWD or severe VWD more often (type 3 in

Table 3. Characteristics of 126 large joint surgeries in 79 VWD patients.

Surgery characteristics	Number/total (%)
Which joint	
Knee	59/126 (47)
Elbow*	9/126 (7)
Ankle	24/126 (19)
Hip	23/126 (18)
Shoulder*	12/126 (10)
Type of orthopaedic surgery	
Joint replacement	26/126 (21)
Hip	17/26
Knee	8/26
Ankle	1/26
Ankle arthrodesis	12/126 (10)
Synovectomy	4/126 (3)
Arthroscopy	55/126 (44)
Surgery in HTC	
Total	76/126 (60)
Surgery because of joint damage after joint bleeds†	
Total	26/110 (24)
Artroscopic	7/26 (27)
Non-artroscopic	19/26 (73)
Prophylactic VWD treatment‡	
Total	88/109 (81)
Artroscopic	37/48 (77)
Non-artroscopic	51/61 (84)
Tranexamic acid	3/109 (3)
Desmopressin	28/109 (26)
Duration (days; median, range)§	1 (1–3)
Clotting factor concentrate	67/109 (62)
Dose (IE FVIII; median, range)¶	9000 (1000–34700)
Duration (days; median, range)¶	5 (1–17)
Combined Desmopressin + clotting factor concentrate	7/109 (6)
VTE prophylaxis LMWH**	30/41 (73)
FVIII monitoring after surgery††	
Total	43/81 (53)
Arthroscopic	12/33 (36)
Non-arthroscopic	31/48 (65)
CFC	40/60 (67)

VWD, von Willebrand disease; HTC, haemophilia treatment center; LMWH, low molecular weight heparin; CFC, clotting factor correction by the use of clotting factor concentrate and/or desmopressin.
*In one case elbow and shoulder surgery was performed during the same operation.
†Unclear in 16 surgeries.
‡Data missing in 17 surgeries.
§Based on 23 cases wherein this information was available.
¶Based on 34 (dose) and 44 (duration) cases wherein this information was available.
**Not documented in most (85/126) surgeries.
††Unknown in 45 surgeries, rarely monitoring on von Willebrand factor levels and if performed always combined with FVIII monitoring.

Table 4. Outcome of 126 large joint surgeries in 79 von Willebrand disease patients.

Outcome after joint surgery	Number/total (%)
Bleeding complication	
Occurrence	23/126 (18); 19/79 pts (24)
Arthroscopic	12/45 (27)
Knee arthroscopy	10/43 (23)
Non-arthroscopic	11/60 (18)
HTC	13/76 (17)
Non-HTC	10/50 (20)
Perioperative CFC	15/88 (17)
No perioperative CFC	7/21 (33)
FVIII monitoring	3/43 (7)
No FVIII monitoring	10/38 (26)
Bleeding treated, total	13/23 (59)
Repeated surgery	1/13
Desmopressin	1/13
Clotting factor concentrate	7/13
Blood transfusion	6/13
Other complication*	17/126 (13)
Joint pain	
Before surgery	79/126 (63)
After surgery	51/126 (40)
Functional impairment	
Before surgery	69/126 (55)
After surgery	48/126 (38)

Pts, patients; HTC, haemophilia treatment centre; CFC, clotting factor correction by the use of clotting factor concentrate and/or desmopressin.
*Including one thrombotic event and inhibitor development in two cases, detailed in Table S2.

15% of vs. 10%, $P = 0.63$, severe VWD 33% vs. 22%, $P = 0.47$). In patients treated with clotting factor concentrates, the mean dose used was higher in those who had a postoperative bleeding according to their medical file (24 567 IE FVIII vs. 9028 IE FVIII, $P = 0.19$). This was due to the necessity of treatment of the bleeding (Table 4). Bleeding complications occurred more often in surgeries in which FVIII or VWF levels were not monitored (10/38, 26% vs. 3/43, 7%; $P = 0.018$). After correction for multiple surgeries within individual subjects, this finding was still significant (OR = 7.8, 95% CI: 1.7, 35.5; $P = 0.007$). This finding was also significant when analysing arthroscopic surgeries separately (6/21 without FVIII monitoring vs. 0/12, $P = 0.041$) but not for non-arthroscopic surgery (4/17, 24% vs. 3/31, 10%, $P = 0.19$). In most cases, documentation on treatment for the postoperative bleeding was found (59%, Table 4). Blood transfusion because of bleeding was documented in six cases, in four hip and two knee surgeries. A thrombotic complication, consisting of pulmonary embolism and an ischaemic cerebrovascular event, was recorded in one obese type 1 VWD patient after an arthroscopic knee operation. This was assumed to be related to the preoperative prophylactic desmopressin infusion (Table S2). The use of low molecular weight heparin (LMWH) prophylaxis was not documented in this case, as in most cases (not documented in 67% of surgeries, 85/126, Table 3).

Discussion

In this large cohort study on VWD in the Netherlands, 14% of the VWD patients reported a history of ankle, knee, hip, elbow or shoulder surgery and 35% of these patients reported bleeding during or after this type of surgery. Subsequent medical file analysis on 126 large joint surgeries in 79 of these patients revealed that previous joint damage due to joint bleeds determined the indication for the joint procedure in 24% of these surgeries. Despite perioperative CFC in 81% of the surgeries, bleeding complications occurred in 24% of the patients.

The strength of this study is that we are the first to report on joint surgery in a large multicenter cohort

of VWD patients, providing information on the occurrence, indications, prophylactic treatment and complications of orthopaedic surgery in VWD patients in daily practice. The results are likely to apply to all moderate to severe VWD patients in the Netherlands, since over 80% of Dutch patients were included in the WiN study. The results probably also apply to most parts of the Western world because of comparable resources and management of VWD. A limitation is the use of a self-administered questionnaire, which may be associated with recall and reporting bias. Since joint aspiration and ultrasound are rarely performed in VWD, we had to rely on the patients and physicians interpretation of joint symptoms to assess postoperative joint bleeding as part of the documented bleeding complications. This issue is partly overcome by reporting both the findings reported by patients as well as documented postoperative bleeds. We could obtain medical file data of a large majority of the patients self-reporting surgery on large joints, in order to validate the findings of the questionnaire. This validation method is however limited by the inherent weakness of missing data in medical files. Nevertheless, patient-reported as well as medical file data point to bleeding complications after orthopaedic surgery of large joints in a large proportion of VWD patients.

Possible explanations for bleeding after orthopaedic surgery in VWD could be anatomic changes after prior joint bleeds, including neovascularization as has been demonstrated in haemophilia, or insufficient CFC [9,10]. A high rate of bleeding complications of 22% after orthopaedic surgery has been reported before in a single centre retrospective case series on 23 VWD patients with 32 orthopaedic procedures. This study also included surgery on smaller joints [7]. Clotting factor consumption seemed to be lower in our series with a comparable rate of documented bleeding complications. However, we recorded treatment for postoperative bleeding in the majority of cases (57%, Table 4) suggesting clinically relevant bleeds in most cases. It is likely that the real life bleeding complication rate is higher because of the inherent flaw of missing data in retrospective medical file studies. Two indications for this assumption are the higher rate of self-reported post-surgical bleeds (self-reported 35% of the patients vs. 24% of patients according to the medical files) and a relatively large proportion of postoperative bleeds was treated with blood transfusion (26%), which would represent grade III bleeding according to the WHO. The finding that 35% of the patients reporting on large joint procedures mentioned bleeding during or after surgery in the questionnaire emphasizes the need for prospective studies to determine optimal prophylactic management of orthopaedic procedures in VWD.

Stringent perioperative coagulation factor monitoring can possibly prevent bleeding complications. No prospective studies have been conducted on the utility of perioperative FVIII and VWF activity monitoring in VWD in relation to the occurrence of postoperative bleeding complications regarding orthopaedic surgery. A pooled analysis of two multicentre prospective clinical studies on pharmacokinetic-guided dosing of VWF/FVIII concentrate in VWD patients undergoing elective surgery, conducted in the USA and Europe, reported haemorrhagic adverse event in 11% and 21% of the subjects respectively. This was despite the fact that overall haemostatic efficacy of the coagulation factor concentrates, as rated by the investigators, was 95% [11]. Experts advise to monitor FVIII and VWF activity for at least a week after major surgery, generally aiming at normalization of these levels in the first 36 h and afterwards at $\geq$50 U dL^{-1} until postoperative day 10–14 [12–16]. Nevertheless, current dosing guidelines do not achieve the increased physiological levels of VWF activity, high molecular weight multimers and FVIII that occur after elective orthopaedic surgery in normal individuals [17]. Furthermore, 24 h laboratory facilities to monitor FVIII and especially VWF activity are not widely available. We recommend that large joint surgery should be performed at specialized HTCs where these facilities, clinicians experienced in VWD treatment and sufficient stock of coagulation factor concentrates are available around the clock. FVIII and VWF monitoring should be performed to optimize dosing.

Our data suggest that bleeding after surgery occurs at least as often after arthroscopic procedures than after non-arthroscopic open surgery. Knee surgery was arthroscopic in most cases (73%) and partial meniscectomy was the most commonly performed operation (51%). Bleeding appeared to occur in 23% of all arthroscopies in our series. A bias towards the inclusion of more complicated arthroscopies cannot be excluded due to the possibility of missing data on uncomplicated surgeries performed in non-HTCs. However, sensitivity analyses did not reveal a difference in self-reported bleeding after orthopaedic surgery between the patients with and without medical file data on orthopaedic surgery (data not shown). Furthermore, 49% (27/55) of the included arthroscopies were performed in non-HTCs. More importantly, a recent systematic review on arthroscopic surgery for knee pain and degenerative knee disease concluded that there is no clear benefit of such surgical procedures, which are merely associated with harm. [18] Therefore, careful consideration should be given to the indication for arthroscopy, especially in patients with coagulation disorders. It is also very important to monitor clotting factor levels in this type of orthopaedic surgery.

Another controversy is the use of prophylactic LMWH after large joint surgery to prevent thrombotic complications. In the Italian series on orthopaedic

surgery in VWD patients, an association between bleeding and the use of anticoagulant prophylaxis was suggested since excessive bleeding occurred in 2/4 cases where this prophylaxis was implemented. They reported no thrombotic complications [7]. We could not reproduce an association between LMWH prophylaxis and bleeding in our series, but found documentation on the use of LMWH prophylaxis in only 41/126 surgeries and can therefore not exclude a harmful effect. In our study, one severe thrombotic event was documented in a patient undergoing knee arthroscopy who was treated preoperatively with desmopressin. This patient had an FVIII level of 93 U dL^{-1} at the time of inclusion in the WiN-study but the FVIII levels at the time of surgery and use of LMWH prophylaxis are unknown. We could not find comparable cases of venous thrombosis after use of desmopressin in literature. Thrombotic complications in VWD patients are rare but, in those reported, associated with orthopaedic surgery and high FVIII levels after the administration of coagulation factor concentrates [19,20]. To avoid very high FVIII levels, it could be theoretically better to use a VWF concentrate with low FVIII content, such as WILFACTIN® (LFB, Les Ulis, France), especially in VWD patients with normal FVIII levels at baseline, but there is no literature to support this practice. Possibly large prospective registry studies on VWD patients that include (orthopaedic) surgery management could resolve the issue on LMWH prophylaxis. Until then, it seems reasonable to at least consider the use of LMWH prophylaxis after VWD is fully corrected with CFC, provided that LMWH prophylaxis would be indicated in routine practice and when other thrombosis risk factors are present or FVIII levels rise above 200 U dL^{-1} [13–16,20].

In conclusion, large joint surgery is reported by 14% of VWD patients. This surgery was related to joint bleeds in 24% and appeared to be associated with bleeding complications frequently, despite prophylactic CFC, both after arthroscopic and non-arthroscopic surgery. Perioperative monitoring of FVIII and VWF activity levels in VWD patients undergoing orthopaedic surgery is strongly advised and may result in less bleeding complications. Prospective studies are needed to determine optimal management of orthopaedic surgery in VWD, including arthroscopy.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. List of relevant comorbidity affecting joint- or muscle function.

Table S2. List of other postoperative complications than bleeding.