Long-term impact of joint bleeds in von Willebrand disease: a nested case-control study

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Supplemental table 1: Pettersson scores from all joints with X-rays

	LE		RE		LK		RK		LA		RA	
Pt/co	Pt	Co	Pt	Co	Pt	Co	Pt	Co	Pt	Co	Pt	Co
n joints	16	9	16	10	38	26	38	26	33	31	33	30
PS 0	15	8	14	10	20	15	23	13	24	31	25	26
PS 1	0	0	0	0	13	7	13	10	2	0	1	3
PS 2	0	1	0		0	2	0	2	1		0	0
PS 3	0	0	0		2	1	0	1	0		0	0
PS 4	0		0		1	1	0	0	0		0	0
PS 5	0		0		1	0	0		1		1	1
PS 6	0		0		0		0		0		0	0
PS 7	0		0		0		0		0		1	
PS 8	0		0		0		0		0		1	
PS 9	0		0		0		0		1		1	
PS 10	0		1		1		0		0		0	
PS 11	1		1		0		0		0		0	
PS 12	0		0				0		0		0	
PS 13							2		4		3	

Supplemental table 1 legend: Abbreviations: PS Pettersson score; Pt VWD-JB patient; co control VWD patient; LE left elbow; RE right elbow; LK left knee; RK right knee; LA left ankle; RA right ankle

Supplemental table 2: results of VWF and FVIII levels after matching VWD-JB patients and VWD controls

	VWF activity centrally measured IU/dL (median, IQR)		VWF activity hist. lowest IU/dL (median, IQR)		FVIII activity centrally measured IU/dL (median, IQR)		FVIII activity hist.lowest IU/dL (median, IQR)	
Match on	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Centr. VWF Act.	**0(0-6)** **n=8**	**6(2-9)** **n=8**	7(4-7) n=8	6(4-9) n=8	2(1-27) n=8	28(22-42) n=8	3(1-4) n=8	23(19-28) n=8
VWF hist. lowest	>50% missing		**3(1-9)** **n=8**	**7(4-9)** **n=8**	>50% missing		6(1-11) n=8	32(24-38) n=8
Centr. FVIII	9(2-15) n=22	8(3-41) n=21	9(4-9) n=22	10(6-21) n=22	**4(2-5)** **n=22**	**4(2-6)** **n=22**	4(1-5) n=22	3(2-4) n=22
FVIII hist. lowest	24(0-86) n=6	44(4-46) n=7	9(4-14) n=10	22(4-27) n=10	51(9-116) n=6	59(22-68) n=7	**31(3-47)** **n=10**	**34(10-49)** **n=10**

Supplemental table 2 legend: Abbreviations: VWF: von Willebrand factor; IQR: interquartile range; FVIII: factor VIII, hist: historically, centr.: centrally measured at the time of inclusion in the Willebrand in the Netherlands study.

The matching outcome is made bold the table. We searched in the Willebrand in the Netherlands study (WiN) cohort, n=804, to find matched controls. As described before (van Galen et al. Haemophilia 2015;21:e185–e192), after matching for age +/- 2 years and sex, we performed FVIII matching on centrally measured FVIII levels if available, otherwise on historically lowest levels +/- 10 IU/dL. We tried to match on FVIII because low FVIII is the most important determinant of joint bleeding in VWD according to the WiN study (de Wee et al. Thromb Haemost 2012;108:683) Most cases (32/48 VWD-JB patients) could be matched on centrally measured or historically lowest FVIII levels.

If no match on FVIII was available within the WiN database, than we matched on VWF severity instead (<10 IU/dL, 10-30 IU/dL, >30 IU/dL based on centrally measured values if available, otherwise (last choice) matching on historically lowest VWF level (VWD severity <10 IU/dL or 10-30 IU/dL VWF activity).

The historically lowest VWF activity had to be ≤30 IU/dL to be included in the WiN study. Because of the low correlation between FVIII and VWF levels and the wide range in age and clotting factor levels within the WiN cohort, the matching procedure caused relatively large differences in the non-matched FVIII and VWF levels between the cases and controls.